SECOND DIVISION, INNER HOUSE, COURT OF SESSION

[2018] CSIH 31
A256/10 & A273/10

Lord Justice Clerk
Lord Brodie
Lord Malcolm

OPINION OF THE COURT

delivered by LORD BRODIE

In the cause

(FIRST) RONALD RICHARDS; and (SECOND) JOHN JARVIE

Pursuers and respondents

against

PHARMACIA LIMITED, c/o PFIZER LIMITED

Defenders and reclaimers

Pursuer: Smith QC, Murray; Lefevre Litigation
Defender: Shand QC, Middleton; DWF LLP

24 April 2018

Introduction

[1] This is a reclaiming motion at the instance of the defenders against an interlocutor of the Lord Ordinary (Lord Beckett) dated 12 May 2017 allowing proof in two actions, one at the instance of Ronald Richards, the other at the instance of John Jarvie. In so far as material to the points which were canvassed before Lord Beckett, the pleadings in the respective actions are almost identical (and certainly intended to be identical). For that reason, having

heard what he describes as in effect one debate on parties' preliminary pleas in the two actions, the Lord Ordinary issued one opinion. We shall follow his example.

[2] As the Lord Ordinary explains in his opinion, these actions are among a number (he mentions a figure of over sixty, we were advised that the number might be about seventy) of actions before the court in which the defenders are being sued in connection with their production, marketing and distribution of the non-steroidal anti-inflammatory drug ("NSAID") celecoxib, manufactured and marketed under the proprietary or brand name of Celebrex. In these two cases the pursuers aver that they each suffered a serious adverse cardiovascular ("CV") event as a result of being prescribed and thereafter ingesting Celebrex. Both pursuers found on fault at common law and separately aver that Celebrex was a defective product giving rise to liability for damage caused, in terms of section 2 of the Consumer Protection Act 1987. It is averred that the defenders are the corporate successors of certain companies in the United Kingdom and in the United States which participated in the research, development and marketing of Celebrex. We were advised during the hearing of the reclaiming motion that Pharmacia Limited is owned by Pfizer Limited and that it has a marketing function within the Pfizer group of companies (the matter is addressed in answers 2.3.1 and 2.3.2). Nothing now turns on precise corporate identity. It is accepted that the pursuers have sued the appropriate defenders. Thus, in the pleadings and in this opinion the expression "the defenders" comprehends all such companies (including companies incorporated outwith the United Kingdom) as had, at the relevant time, responsibility for the acts and omissions relied upon by the pursuers as giving rise to liability to make reparation to them.

[3] Celebrex 100 mg and 200 mg capsules received marketing authorisation in the United Kingdom in May 2000. Mr Richards took Celebrex as prescribed between July 2002

and May 2004. Mr Jarvie took Celebrex as prescribed between May 2002 and December 2004.

[4] A number of acronyms appear in this opinion. They are listed with an explanation of what the letters stand for in the appendix.

Procedure

[5] Rule 2.2 of the Rules of the Court of Session empowers the Lord President, where he is of the opinion that an aspect of the procedure which would otherwise apply to particular proceedings, or proceedings of a particular description, is unsuitable for the efficient disposal of those proceedings, to direct that that aspect of the procedure is not to apply in respect of those proceedings and that such other procedure as he directs is to apply instead. Such a practice direction was made on 23 September 2010 in respect of actions of which the actions at the instance of Mr Richards and Mr Jarvie are examples. It is "Practice Direction No 2 of 2010: Personal Injury Actions relating to the drugs Vioxx and Celebrex". It relates both to actions already raised as at 23 September 2010 and to actions raised subsequently ("new actions").

[6] Among other provisions, Practice Direction No 2 of 2010 provides that chapter 43 of the Rules of Court shall not apply and that a new action shall be raised as an ordinary action. The action at the instance of Mr Richards and the action at the instance of Mr Jarvie had been raised prior to the making of the practice direction. The actions therefore became subject to the practice direction on 23 September 2010 but its provisions were to an extent anticipated on 26 May 2010 when on the motion of the pursuers of consent these two actions were withdrawn from the procedure under chapter 43 of the Rules of Court, appointed to

proceed as ordinary actions and sisted "pending consideration of further procedure in this and related cases."

[7] The objective of Practice Direction No 2 of 2010 can be seen from its paragraph 11: "The court will manage the actions with the aim of securing the efficient disposal of them." To that end the court was given the powers set out in paragraph 12 and 13. These powers include, either acting on the court's own initiative or on the motion of one or more parties: power to determine future procedure; power to set timetables; power to order disclosure of information; power to order production and recovery of documents; and power to order production of expert reports and affidavits. Paragraph 14 provides that where reasonably practicable the court's management function will be discharged by a particular Lord Ordinary. Mr Smith QC, who has represented the pursuers from the beginning of these litigations and who appeared before us, observed that the making of Practice Direction No 2 of 2010 was comparable to the making of a group litigation order in England, as provided for by Civil Procedure Rule 19.11 (as to which see *Blackstone's Civil Practice 2017* para. 14.66 *et seq*). We have noted that information but, for present purposes at least, nothing would appear to arise from it.

[8] Consideration of the 35 or so interlocutors pronounced in Mr Jarvie's action between the making of the practice direction and the action coming before Lord Beckett for debate in March 2017 does not suggest that this and the other actions subject to Practice Direction No 2 of 2010 have proved capable of very efficient, at least in the sense of swift, disposal. The Minute of Proceedings points to difficulties over disclosure of information and recovery of documents, a matter alluded to by Mr Smith. Mr Smith was able to provide some additional information. In 2010 the "related cases" included actions against Merck Inc. arising out of the prescription of a similar drug to Celebrex which was marketed under the

proprietary name of Vioxx. Merck had initially taken the lead in presenting a defence to what at one point had been in excess of 200 cases. Some of these cases involved pursuers who had been prescribed both Celebrex and Vioxx. The Merck cases eventually settled. The cases against the defenders have not. By interlocutor of 9 July 2012, in discharge of a duty imposed by paragraph 15 of the practice direction to give early consideration as to whether, in order to determine or give guidance on any generic issue in the actions, it is appropriate to identify a lead action or actions to be progressed at an advanced rate, the actions at the instance of Mr Richards and Mr Jarvie, together with one other action, were appointed to be lead actions. That of Mr Richards was selected to represent the cases where the pursuer had suffered a heart attack. That of Mr Jarvie was selected to represent the cases where the pursuer had suffered a stroke. The third action was one where the pursuer (who has subsequently died) had been prescribed both Celebrex and Vioxx. The pleadings in the lead actions were adjusted with a view to encompassing what were seen to be the common issues over the whole group of Practice Direction No 2 of 2010 cases. On 7 July 2016 the action at the instance of Mr Richards and that at the instance of Mr Jarvie were appointed to a Procedure Roll debate.

Regulatory approval of medicinal products

[9] These actions are concerned with the safety or otherwise of medicinal products available only on prescription. Parties' respective averments make reference to the process for the regulation of medicinal products and in particular the interaction between the defenders and the authorities responsible for marketing authorisation. That process provides the broad context of the litigations and their pleadings and it might therefore be useful at this stage to say something about it.

[10] As appears from the pleadings, medicinal products may not be placed on the market anywhere in the EU unless they have been granted an appropriate licence or marketing authorisation. The same is true in the United States of America. We were referred to Powers & Barton, *Clinical Negligence* (5th edit) paras 13.1 to 13.54 for a summary of the regulatory framework for medicines in the United Kingdom. The fifth edition of Powers & Barton was published in 2015 and the text reflects the position as at that date, but it also touches on the history of regulation. This allows a broad understanding of the regime which was in force when the pursuers in these two actions were being prescribed Celebrex.

[11] The methodical implementation of mechanisms to promote the efficacy and safety of medicinal products may be referred to as "pharmacovigilance". Powers & Barton describe pharmacovigilance within the EU as a tri-partite operation. By that they mean that (1) EU institutions, (2) the competent authorities of Member States and (3) the parties authorised to market medicinal products ("marketing authorisation holders") all have responsibilities in the matter, both at the stage of application for necessary regulatory approvals and thereafter. As counsel confirmed before us, although the fact that Celebrex had all necessary regulatory approvals in the United Kingdom is relevant to a consideration of the issues in these and the other Practice Direction No 2 of 2010 cases, it is not suggested that regulatory approval can absolve the defenders of their responsibilities in relation to the marketing of the drug.

[12] At the European level, pharmacovigilance has a history extending back to at least 26 January 1965 and the adoption of Council Directive 65/65/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products. Further provision was made by Council Directives 75/318/EEC and 75/319/EEC. Article 50 of Council Regulation (EEC) 2309/93 established the European Agency for the Evaluation of Medicinal Products ("EMEA"). The EMEA comprised the

Committee for Proprietary Medicinal Products ("CPMP"), the Committee for Proprietary Veterinary Products, a secretariat, a director and a management board. The CPMP was responsible for the preparation of the opinion of the EMEA on any question relating to the evaluation of medicinal products for human use. That structure was superseded on implementation of Regulation (EC) 726/2004 of the European Parliament and Council of 31 March 2004. In place of the EMEA there was established the European Medicines Agency. There was also established, as part of the Agency, the Committee for Medicinal Products for Human Use ("CHMP"). The CHMP assumed the responsibilities of the former CPMP. Despite being re-established as the European Medicines Agency, Powers & Barton tell us (at para 3.18 (1)) that the Agency retained the acronym EMEA until December 2009. It is now however referred to as the EMA.

[13] Among the functions of the EMA is the issue of marketing authorisation for a number of specified medicinal products, but more generally the issue of marketing authorisation remains a matter for the competent authorities of the Member States. In the United Kingdom the competent authority is (and at all relevant dates has been) the "licensing authority" provided for by section 6 of the Medicines Act 1968. The licensing authority is a body composed of the Ministers specified in section 1 of the 1968 Act. As Powers & Barton explain at para 13.19, the licensing authority carries out its executive functions through a body ("the regulatory authority") which was created for the purpose of regulating all the activities related to human medicinal products in the United Kingdom including the grant, renewal, variation, suspension and revocation of licenses and certificates. The regulatory authority was originally a branch of the then Department of Health and Social Security and was known as the Medicines Division. The Medicines Division was reorganised in April 1989 into an agency known as the Medicines Control

Agency ("MCA"). The MCA was the regulatory authority (and therefore, from the European perspective, the competent authority of the United Kingdom as a Member State) from April 1989 until April 2003 when it was again reorganised following a merger with the Medical Devices Agency as the Medicines and Healthcare Products Regulatory Agency ("MHRA").

[14] Until 2012 the statutory framework for the domestic regulation of medicinal products was provided by the Medicines Act 1968 as amended by the Medicines Act 1971. Provision was made for the grant and renewal of product licences, manufacturer's licenses and wholesale dealer's licences, without which the relevant activity was prohibited. Section 18 of the 1968 Act provided that applications for licences should be accompanied by such information as may be prescribed by subordinate legislation. In 2012 much, although not all, of the 1968 Act was repealed and its provisions relating to the regulation of medicinal products replaced by provisions of the Human Medicines Regulations 2012, SI 2012/1916.

[15] In the United Kingdom the regulatory function is supplemented by the advice given to Ministers and the licensing authority by advisory committees established under the 1968 Act. One such was the Committee on Safety of Medicines ("CSM"). The CSM was replaced in 2005 by the Commission on Human Medicines ("CHM"). The functions of the CHM are now set out in article 10 of the 2012 Regulations.

[16] While regulation of medicinal products is, and at all relevant dates has been, within the competence of Member States and therefore in the United Kingdom a matter for the licensing authority acting through the regulatory authority for the time being, that regime has of course been subject to the relevant European measures. Directive 2001/83/EC of the European Parliament and of the Council, dated 6 November 2001, provided a detailed and extensive Community Code Relating to Medicinal Products for Human Use. Article 6 of the

Directive provides that no medicinal product may be placed on the market of a Member State unless a marketing authorisation has been issued by the competent authorities of that Member State or an authorisation has been granted by the EMA in accordance with Regulation (EEC) 2309/93. The marketing authorisation holder shall be responsible for the marketing of the medicinal product. In terms of article 8 of the Directive the application for marketing authorisation submitted to a competent authority must be accompanied by certain particulars and documents. The particulars and documents include therapeutic indications, contra-indications and adverse reactions; the results of pharmaceutical tests, pre-clinical tests and clinical trials; a Summary of Product Characteristics ("SPC") in accordance with article 11; a mock-up of the outer packaging containing the details provided for in article 54 and of the immediate packaging of the medicinal product containing the details provided for in article 55; and a package leaflet in accordance with article 59.

[17] Powers & Barton say this of SPCs (at paras 13.30 and 13.33):

> "13.30 The data sheet or summary of product characteristics (SPC) is designed and intended to provide the physician with the key information necessary for the safe and effective use of the medicine. Critically it is a dynamic document that evolves with time as experience with the wider use of the medicine concerned increases and better defines its efficacy and safety and any population at risk. For all practical purposes, it is the most important regulatory document relating to a medicinal product.
>
> …
>
> 13.33 Copies of SPCs are made available to healthcare professionals from reference sources such as the Association of the British Pharmaceutical Industry (ABPI) Data Sheet Compendium or monographs which are usually updated annually. In addition, since 1999 SPCs and PILs (see below) have been available to healthcare professionals online at a dedicated website updated daily known as the electronic Medicines Compendium. All information on the website is provided by pharmaceutical companies and is approved by the regulatory authorities."

[18] The acronym "PILs" which appears in para 13.33 of Powers & Barton refers to Patient Information Leaflets, otherwise package leaflets as provided for by article 59 of the

Directive. Article 59 provides that the PIL shall be drawn up in accordance with the SPC. Certain information must appear in the PIL. This includes contra-indications, appropriate precautions for use and special warnings. Powers & Barton provide this commentary on PILs at paras 13.34 and 13.35:

> "13.34 A patient information leaflet (PIL) is 'a leaflet containing information for the user which accompanies a medicinal product' which provides the patient with the key information necessary for the safe and effective use of the medicine. It is not promotional. The language must be simple and non-technical, easily readable and readily understood by lay people. The amount of information that is included calls for a delicate balance between the provision of adequate information to support patients using the medicine appropriately and excessive information which may dilute other important messages in the text. Furthermore, the wording of the PIL should encourage appropriate use and adherence to treatment without giving rise to anxiety or unnecessarily frightening the patient.
>
> 13.35 With changing attitudes to the provision of information directly to the patients, PILs have, over the years, become progressively more detailed. …Over time, as increased weight has been placed on the active involvement of patients in decisions regarding their own health, there has been a trend towards the provision of more detailed information in PILs. The current requirements are set out in the Human Medicines Regulations 2012, Part 13, together with Schs 24 and 27."

[19] The adoption of Directive 2001/83/EC and with it the Community Code Relating to Medicinal Products for Human Use, post-dates the issue of marketing authorisation for Celebrex but, at least in part, the Directive's provisions reflect pre-existing European measures. SPCs and PILs are not of recent provenance. Provision for the contents of SPCs was made by the amendment to Council Directive 65/65/EEC effected by Council Directive 83/570/EEC of 26 October 1983. There is reference to a package leaflet in the original text of the 1965 Directive.

[20] As Powers & Barton's reference to the SPC as a "dynamic" document illustrates, the process of communication between those marketing medicinal products and the licensing authority is not expected to come to an end on the grant of a marketing authorisation. This

is addressed in title IX (articles 101 to 108) of Directive 2001/83/EC. Powers & Barton provide this short summary of the relevant provisions at para 13.18 (3):

> "The marketing authorisation holder must operate its own pharmacovigilance system, evaluate all information scientifically, consider options for risk minimisation and prevention and take appropriate measures as necessary: including, *inter alia*, an appropriately qualified person responsible for pharmacovigilance; a pharmacovigilance master file; and a risk management system for each medicinal product, monitoring and updating the risks."

The pursuers' cases

Celebrex

[21] Inflammation of tissue is productive of pain. Inflammation and its associated pain can become chronic, as is the case with, for example, osteoarthritis and rheumatoid arthritis. These conditions are widespread, particularly in more elderly populations. NSAIDs reduce inflammation by blocking the action of a protein that acts as an enzyme, cyclo-oxygenase 2 ("COX-2"). However, traditional or standard NSAIDs, such as Aspirin or Ibuprofen, also block the action of another protein that acts as an enzyme, cyclo-oxygenase 1 ("COX-1"), a catalyst for the production of prostaglandins which promote the production of the natural mucus lining which protects the stomach. The blocking or suppression of COX-1 can therefore result in harmful gastro-intestinal effects, including the development of ulcers and internal bleeding.

[22] In about 1991 a method was discovered of producing a NSAID which would suppress only COX-2 thereby avoiding the adverse consequences of suppressing COX-1. Such NSAIDs may be described as COX-1 sparing analgesics, or as selective COX-2 inhibitors. Among these was one developed by the defenders (or at least the rights to which were acquired by the defenders) which had as its generic name celecoxib and which was marketed as Celebrex. Another such NSAID was developed by Merck Inc. and was

marketed as Vioxx. The defenders also acquired the rights to a similar COX-1 sparing analgesic with the proprietary name of Bextra.

[23] On 29 June 1998 the defenders applied to the United States Center for Drug Evaluation and Research for approval to market Celebrex in the United States under reference number NDA 20-998. The proposed indication for use of the drug was treatment of the symptoms of osteoarthritis and rheumatoid arthritis. The application stated that celecoxib had greater efficacy and safety than currently available NSAIDs.

[24] The first marketing authorisation for Celebrex in the EU was granted by the Swedish Medical Products Agency on 3 December 1999. As noted above, Celebrex 100mg and 200mg capsules received marketing authorisation in the United Kingdom in May 2000. The relevant marketing authorisation numbers were PL 08821/0057 and PL 08821/0058 respectively. Celebrex first appeared in the British National Formulary in September 2000 (volume 40).

[25] On 30 September 2004 Vioxx was withdrawn from the market. In November 2004 the defenders included a "black box warning" in the PIL for Bextra. A black box warning is the highest level of warning that can be inserted prior to a product being withdrawn from the market. On 7 April 2005 a Pfizer company agreed to insert a black box warning on the Celebrex label in relation to products marketed in the United States. It stated: "Celebrex may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction and stroke which can be fatal."

[26] Celebrex continues to be authorised to be marketed in Scotland and throughout the EU.

Injury

[27] Mr Richards was born in 1944. He has a medical history of soreness and stiffness in

his joints albeit he has enjoyed an active lifestyle. In 1996 he was referred to a rheumatoid clinic but, after testing, no diagnosis was made. He had been prescribed various painkillers for his condition, including Voltarol, Diclofenac and Naproxen. On or about 3 July 2002 he was prescribed Celebrex by his general medical practitioner. The prescribed dosage was 200 mg per day. His GP explained to Mr Richards that Celebrex was a new drug and that there had been positive reports about it. He said that Mr Richard's dose of Naproxen was getting too high and that it did not work as well as Celebrex did. Mr Richards accepted the advice to take Celebrex. In the event, Celebrex was effective in treating his joint soreness and stiffness. Mr Richards took it every day. On 12 May 2004, he suffered a heart attack.

[28] Mr Jarvie was also born in 1944. He has long-standing cervical and lumbar spondylosis. He was medically retired from work as a coal miner in 1990 as a result of that condition. He regularly took analgesia for back pain. He had oesophagitis. He was advised not to take Diclofenac. On 4 January 2001, Mr Jarvie was examined by his GP. His GP prescribed Vioxx. At a review on 1 February 2001, Mr Jarvie complained that Vioxx caused him bloating. The prescription was not renewed. On or about 3 May 2002, Mr Jarvie saw his GP. He had pain in his left arm, elbow and shoulder. At a further consultation on 31 May 2002, the GP prescribed Celebrex. Mr Jarvie took the prescribed dose of 200 mg Celebrex each day between 31 May 2002 and 3 December 2004. He found Celebrex to be helpful in moderating his pain. On 21 November 2003 Mr Jarvie suffered a stroke. He suffered a second stroke on 11 May 2004.

[29] The pursuers have averments (at statement 2.6) of the mechanism whereby selective inhibition of the COX-2 enzyme can lead to a CV event. Selective inhibition interferes with the production and operation of prostacyclin rendering the formation of blood clots more likely. Prostacyclin acts to prevent platelet formation and the clumping that is involved in

clotting. Increased risk of clots causes an increased risk of stroke or myocardial infarction. As was confirmed to the Lord Ordinary during the debate before him, it is the pursuers' position that the ingestion of Celebrex over a significant period caused (in the sense of materially contributed to), in Mr Richards's case, his heart attack on 12 May 2004 and, in Mr Jarvie's case, his strokes on 21 November 2003 and 11 May 2004. Before the Lord Ordinary counsel for the defenders stated that he apprehended that the pursuers would attempt to prove causation of injury on an analysis comparable to that approved by the House of Lords in *Fairchild* v *Glenhaven Funeral Services Ltd and Ors* [2003] 1 AC 32 (material increase in risk being sufficient to satisfy the causal requirements for liability) but counsel for the pursuers explicitly disclaimed any such intention. Mr Smith confirmed that position before us. The pursuers accept that they will have to satisfy the onus of establishing that the particular adverse CV events affecting them were, on a balance of probabilities, caused (on a "but for" basis) by their long-term ingestion of Celebrex.

Liability

[30] The pursuers' case is of failure on the part of the defenders to provide adequate information as to a material risk of the association of adverse CV events with long-term consumption of Celebrex. It is presented on two bases: (1) negligence; and (2) liability for damage by virtue of section 2 (1) of the Consumer Protection Act 1987. Immediately following the averments at statement 2.6 as to the mechanism whereby ingestion of selective COX-2 inhibitors such as Celebrex may lead to an adverse CV event, the pursuers aver that the increased risk of stroke or myocardial infarction is a material risk, in the sense of a more than *de minimis* risk. It is averred that patients taking Celebrex who were not previously at risk could become at risk by reason of their ingestion of the drug and that those already at risk could become subject to an increased risk. It is averred that from 1999 onwards the

defenders had evidence that Celebrex was implicated in a significant and materially increased risk of serious cardiac side effects but that the dangers were not disclosed until January 2005.

[31] In statement 6 of the condescendence in each of the Records the pursuers aver that their injury was caused by fault and negligence on the part of the defenders. They aver that their respective GPs reasonably relied on the defenders to disclose information of any known risks, dangers or side effects of the drug and that the defenders knew or ought to have known that they would so rely. They aver that the defenders knew or ought to have known that Celebrex carried the risk of increased CV events for long-term users. The defenders accordingly had a duty to bring such a risk to the attention of consumers and medical practitioners whereas they did not do so until after the pursuers had stopped taking the drug. The pursuers aver that had the defenders fulfilled the duties incumbent upon them the pursuers' GPs would not have prescribed Celebrex and the pursuers would not have suffered loss and damage. Moreover, as it was not possible for GPs properly to advise their patients of the risk of serious adverse CV events, the pursuers were prevented from giving informed consent to a decision by the GP to prescribe Celebrex.

[32] Section 2 (1) of the Consumer Protection Act 1987 provides that where any damage is caused wholly or partly by a defect in a product, the producer of the product, any person who has held himself out to be the producer of the product, and the importer of the product, shall be liable for the damage. Put shortly, in terms of section 3 of the Act there is a defect in a product if the safety of the product is not such as persons generally are entitled to expect. The pursuers aver that, as a pharmaceutical product marketed without information being provided as to CV risk, Celebrex was defective.

The Lord Ordinary's decision

[33] The Lord Ordinary discusses the submissions that he had heard under the respective heads of relevancy and specification. Looking first at the common law case his assessment is that while the pleadings are lengthy and detailed, and might in places be viewed as straying from giving notice of lines to pleading evidence, the essence of the common law case is relatively simple. In the view of the Lord Ordinary the pursuers sufficiently identify the medical events they found on as giving rise to their loss. They identify the duties said to have been breached and how those breaches led to the pursuers taking Celebrex on prescription. They aver that but for the ingestion of Celebrex, they would not have suffered the loss, injury and damage for which they seek reparation. It is apparent from the pleadings that each pursuer aims to prove that his consumption of Celebrex caused, in the sense that it made a material contribution to, the medical event(s) on which he founds. Accordingly, it cannot be concluded at this stage that should the pursuers establish all that they seek to prove, still their case at common law must fail. The Lord Ordinary's conclusion is the same in relation to the case based on the Consumer Protection Act.

[34] The Lord Ordinary heard an argument premised on what was said by Lord Macfadyen in *Royal Bank of Scotland* v *Holmes* 1999 SLT 563 and *Buchanan (Stewart) Gauges Ltd* v *BEC (Scotland) Ltd* 2001 GWD 3-126 on what was required when pleading a case of fraud. Twenty one passages from the pursuers' pleadings were identified by the defenders as examples of instances where fraud (or at least deliberate wrongdoing) was averred and subjected to the criticism that the pursuers do not given sufficient notice of who was responsible for the act, omission or representation complained of; what it consisted of; when it was done and in what circumstances. The Lord Ordinary was unimpressed by these

criticisms except in one instance. With the excision of that one passage he accordingly allowed parties, before answer, proof of their respective averments.

The Grounds of Appeal

[35] The defenders present three grounds of appeal (albeit in four paragraphs, the first of which being a general statement to the effect that the Lord Ordinary erred by allowing proof before answer). Renumbered and with numbers substituted for bullet points to indicate subordinate paragraphs, the grounds of appeal may be stated as follows:

> 1. The Lord Ordinary has erred in holding that the case of alleged common law negligence is relevant and sufficiently specific to merit enquiry at proof before answer. In particular:
>
> 1.1 The case pled against the defenders at common law is that they breached a duty to "bring any known defects, risks, dangers or side effects of the drug to the attention of consumers and medical practitioners." The pursuers do not aver what are the specific "defects, risks, dangers or side effects" to which they refer. While they make various averments about what various studies allegedly showed about cardiovascular risks, these averments, in so far as sufficiently specific, do not pass the test of relevancy, and otherwise do not give the defenders fair notice of what the pursuers intend to prove by them.
>
> 1.2 An averred duty to warn of a risk which did not in fact eventuate is irrelevant: *BPE* v *Hughes Holland* [2017] UKSC 21. In the absence of notice of what is the "risk" of which the pursuers contend notification should have been given and an offer to prove that that particular risk materialized in the case of the pursuers, the pursuers' pleadings are irrelevant on that ground also.

1.3 The pursuers do not aver by what means and in what terms the defenders had a duty to "bring any known defects, risks, dangers or side effects of the drug to the attention of consumers and medical practitioners." In the absence of averments about what should have been the terms of the alleged notification of whatever alleged "defects, risks, dangers or side effects" the pursuers found on, by what means the notification should have been made, and to whom notification by that means should have been directed, the pursuers are not in a position to lead evidence of a causal connection between any alleged injury suffered by them and the duty averred.

2. The Lord Ordinary erred in holding that the case based on the provisions of the Consumer Protection Act 1987 is relevant and sufficiently specific to merit enquiry at proof before answer. In particular:

2.1 All medicines have side effects. Consumers of a pharmaceutical medicinal product are not entitled to expect that such a product will be free from risk: *Wilkes* v *Depuy International Limited* [2016] EWHC 3096 (QB). The pursuers fail to specify what is the defect upon which they found. They fail to specify in what way Celebrex was not as safe as persons generally were entitled to expect. The averment that "Persons consuming Celebrex, including the pursuer, were entitled to expect that it would not carry the high risk of adverse cardiovascular events, such as that which befell the pursuer and as herein condescended on" does not give fair notice of what persons generally are entitled to expect. "Persons generally" do not know the pursuers or what happened to them, and the events which occurred to each pursuer were different from that which occurred to the other. John Jarvie avers he experienced two strokes. Ronald

Richards avers that he suffered a heart attack. John Jarvie does not offer to prove that Celebrex causes strokes, nor (if that is his case) does he offer to prove at what dosage Celebrex causes strokes. Ronald Richards does not offer to prove that Celebrex causes heart attacks, nor (if that is his case) does he offer to prove at what dosage Celebrex causes heart attacks. The reference to "the high risk of adverse cardiovascular events such as .... hereinbefore condescended on" is irrelevant and lacking in specification for the same reasons as the common law case is irrelevant and lacking in specification. The pursuers are not in a position standing their pleadings to lead evidence of a defect in Celebrex.

2.2 In circumstances where John Jarvie does not offer to prove that Celebrex causes strokes, and in particular does not offer to prove that it causes strokes at the dosage at which it was prescribed for him, his averments are not habile to instruct a case that the alleged injury which occurred to him was caused by a defect in Celebrex. In circumstances where Ronald Richards does not offer to prove that Celebrex causes heart attacks and in particular does not offer to prove that it causes heart attacks at the dosage at which it was prescribed for him, his averments are not habile to instruct a case that the alleged injury which occurred to him was caused by a defect in Celebrex. The pursuers aver in article 7 of condescendence that: "Had the warnings been provided from the outset, few if any doctors in the UK would have prescribed the medication." However on the pursuers' pleadings the defect under the 1987 Act upon which they found is not the absence of warning. Thus the pursuers aver "Not only was the product defective, the defenders knew it to be so. If it was not defective, they would not have required to alter the warnings on the packaging to a material effect as they

did." Accordingly, whatever alleged (unspecified) defect in Celebrex the pursuers found on they cannot establish that even if it existed and was a "defect" within the meaning of the 1987 Act it caused their loss.

2.3 If (contrary to their averments in the first part of article 7 of condescendence) the alleged defect on which the pursuers rely is some alleged deficiency in warning, the pursuers' case under the 1987 Act is not relevantly pled as a case where the alleged defect in Celebrex founded on was a deficiency in warning. Further the pleadings do not give notice of what was the alleged deficiency in warning, if any, upon which the pursuers found. Such specification is necessary to determine whether any such alleged deficiency of warning constitutes a defect within the meaning of the Act; and is central also to the question of whether or not the pursuers can establish causation: *Worsley* v *Tambrands* [2000] P.I.Q.R. P95. In the absence of such specification the pursuers are not in a position to prove to whom the warning(s) should have been directed nor what the terms of such warnings should have been nor what the effect thereof would have been, if any, on the prevention or otherwise of the strokes and heart attack suffered by John Jarvie and Ronald Richards respectively.

3. The Lord Ordinary has erred in holding that the pursuers' averments anent fraud and deceit on the part of the defenders provide the defenders with fair notice of the case made against them and that they are sufficiently specific and relevant as to merit enquiry. *Esto* said averments are sufficiently specific *per se* (which is denied), on the basis of concessions at the Bar by Senior Counsel for the pursuers that fraud is incidental to the issue before the court, they are, in any event, extraneous and

irrelevant to both of the grounds of action in these litigations. They should therefore not have been admitted to probation: *JD* v *Lothian Health Board* [2017] CSIH 27.

Submissions

Defenders

[36] On behalf of the defenders, Ms Shand QC adopted her revised note of argument. She pointed to the pursuers' averments that they had each been prescribed Celebrex at the United Kingdom approved dosage of 200mg per day. However, despite a variety of formulations adopted in their averments about increased risk under reference to a number of studies, the pursuers did not aver that there was a statistically significant increased risk of adverse CV events at that dosage. The studies referred to included those which involved dosages of up to 800mg per day. An averment quantifying the increase in risk was important for a determination of whether or not there was a duty to provide a warning, the terms of such a warning, to whom it should be given and whether or not a supposed breach of that duty actually caused the loss claim, it being for the pursuers to aver that the adverse CV events which they suffered had indeed been caused by the ingestion of Celebrex at the United Kingdom approved therapeutic dose. The essence of the defenders' argument before the Lord Ordinary was that the pursuers had not pled a relevant case of negligence based on a supposed duty to warn. The Lord Ordinary had not properly analysed that argument. He had failed to recognise that the viability of the propositions which he saw as encapsulating the essence of the pursuers' cases depended on the underlying detail of: (i) what level of risk was known to or ought to have been known to the defenders; (ii) what was the specific risk about which the defenders were under a duty to warn and in what terms such a warning ought to have been given; and (iii) what would have happened relative to the occurrence of

CV events suffered by the pursuers if such a warning had been given. The pursuers had not provided the necessary specification by reference to what factor they alleged the risk to be increased. They had accepted (at statement 2.3) that the relevant SPC did advise that among the very rare side effects of Celebrex was a "less than 1 in 10,000 risk of heart failure and myocardial infarction". The pursuers do not aver what different warning should have been given. They had failed to give fair notice of their case: cf *Argyll & Clyde Health Board* v *Strathclyde Regional Council* 1988 SLT 381 at 383. It was no answer to say, as the Lord Ordinary records had been said at the Procedure Roll debate, that expert witnesses would be able at proof to explain the inferences to be drawn from the studies. If there are inferences which will be relied on, they should be averred.

[37] As with the common law case, when addressing the statutory case under the Consumer Protection Act 1987, the Lord Ordinary had failed properly to analyse the detailed criticisms of the pursuers' averments as to "increased risk" or "high risk", which was the foundation of the statutory case. No medical product is 100 per cent safe and accordingly the pursuers cannot expect 100 per cent safety: *Wilkes* v *Depuy International Limited* [2018] 2 WLR 531 at paras [13], [14] and [65]. The defenders were entitled to know why the pursuers said that Celebrex was defective. It was not clear whether their case related exclusively to lack of appropriate warnings or whether the complaint was that there was something intrinsically wrong with the drug. If it were the latter what was said to be wrong is not specified; if it were the former the required warning, absence of which made the drug defective, is not specified. If, as appeared to be the case, the pursuers did not know in what terms a warning should have been given, they are not in a position to establish that had a warning been given the drug would not have been prescribed and therefore that the pursuers would not have taken it. The context was that while regulatory approval (which

had been given here) is not an automatic defence it is nevertheless powerful evidence that the level of safety which people generally were entitled to expect had been achieved. Moreover, there was no offer to prove the level of risk associated with the alternative treatment which the pursuers would have undertaken had they not been prescribed Celebrex.

[38] In any event, the pursuers' numerous averments of fraud and deceit are irrelevant and should be excluded from probation and that for two reasons. First, it was conceded on behalf of the pursuers before the Lord Ordinary that fraud was incidental and extraneous to the issue before the court and not an essential fact which had to be established. Second, even if potentially relevant the averments in question were not sufficiently specific to give the defenders the requisite high degree of notice which is appropriate with an allegation of fraud.

Pursuers

[39] The motion made by Mr Smith QC on behalf of the pursuers and respondents was to refuse the reclaiming motion and to adhere to the interlocutor of the Lord Ordinary, appointing the cause to a diet of proof before answer. Properly analysed, the criticisms made of the pursuers' pleadings fell into four categories: (i) statistics; (ii) warnings; (iii) causation; and (iv) fraud. Mr Smith explained that he would address each of these but, by way of giving context, he began by drawing the court's attention to the importance for the system of statutory regulation which is to be attached to the content of SPCs and PILs: cf Powers & Barton, *Clinical Negligence* (5th edit) para 13.17.

[40] Much of what the defenders had complained of was not a lack of essential specification, rather it related to a level of forensic detail which is misplaced at debate. The plea of lack of specification finds its proper application in a case where a defender does not

know the case to be made against him and objects to being taken by surprise at the proof: *Macdonald* v *Glasgow Western Hospitals* 1954 SC, per LP Cooper at 465; *JD* v *Lothian Health Board* [2017] CSIH 27, per Lord Glennie at [72]. Criticism on lack of specification should be proportionate. That advanced by the defenders was not. The defenders had been given fair notice. The Lord Ordinary's analysis at para [42] of his opinion was correct. The pursuers' pleadings met the test of relevancy: *Jamieson* v *Jamieson* 1952 SC (HL) 44.

[41] Turning to the part of his submissions which Mr Smith headed "statistics", he pointed to the pursuers' averments about drug trials demonstrating an increased risk of adverse CV events at therapeutic levels (upwards of 100 mg per day). Indeed there is an averment that in studies conducted by the defenders on patients with arthritis the estimated rate (of onset of a CV event) ratio exceeded 2 at a dose of 100mg and exceeded 3 at a dose of 400mg, but in any event it could not be said that the results of trials at higher levels were irrelevant to demonstrating the probability of adverse events. Unless otherwise indicated, increase in risk meant increase over a placebo or no administration at all. Contrary to the defenders' submission it was not necessary for the pursuers to aver the actual level of enhanced risk to which they as individuals were exposed; that is a medical and scientific impossibility. It was sufficient that they averred, as they did, that the increased level of risk was a material risk. This was consistent with the issue in 2005 by the EMEA of urgent safety restrictions for COX-2 inhibitors on having obtained further data from the defenders. It was not the function of the court to determine an absolute level of risk to which the pursuers were exposed. The judge is not required to search for medical certainty: *Elvicta Wood* v *Huxley* [2000] WL 664536, 19 April 2000. To use the language of Mackay J in *XYZ* v *Schering* [2002] EWHC 1420, the place of the court was not in the forest of epidemiology but in the open country where the simpler concept of balance of probabilities rules.

[42] On warnings, it was the pursuers' case, as they had averred, that the defenders ought to have included a warning on the SPC provided to the regulatory authorities and all later approved versions of the SPC, whereas no proper warnings were provided. Again as averred, it was the public, and particularly prescribing doctors and their patients, who should be warned. The content of the warning should have reflected the results of the studies which were available to the defenders. What appeared on the "black box" warning which the defenders agreed on 7 April 2005 with the United States Food and Drug Administration to include in the Celebrex label would have provided a good model, but the pursuers' case was that what was required were words to the effect that consumption of Celebrex involves a significant increase in CV risk. No such warning was given by the defenders prior to the pursuers suffering their respective adverse CV events.

[43] As to causation, Mr Smith confirmed that, as they had pled, the pursuers intended to prove that their respective GPs would not have prescribed Celebrex had a warning of the material risk of adverse CV events been given, indeed if that warning had been given from the outset they say that few if any doctors in the United Kingdom would have prescribed it. In the result patients were prevented from giving informed consent. The pursuers further intended to prove that had they not taken Celebrex they would not suffered adverse CV events. The evidence for that would be a combination of medical evidence as to mechanism and statistical evidence as to likelihood of an adverse CV event given the increased risk associated with Celebrex. The Lord Ordinary had correctly understood the pursuers' cases as appeared from paragraph [43] of his opinion.

[44] Turning finally to the averments of fraudulent conduct on the part of the defenders which are discussed by the Lord Ordinary at paragraphs [57] to [84] in his opinion, Mr Smith confirmed that he was not making a case of fraud as such; he had no plea which

would support such a case. That did not mean that they were irrelevant. The Lord Ordinary, before whom the defenders had attacked these averments as lacking in specification, had been correct to admit all but one sentence of them to probation. It was the pursuers' case that the defenders knew their product was defective in the sense of carrying a material risk of adverse CV events when taken in therapeutic doses. That the defenders did not disclose that fact and were accordingly responsible for *suppressio veri* or *suggestio falsi* was a legitimate line of evidence. It was plainly relevant to proving that a product is defective for evidence to be led that the defenders knowingly omitted data or information concerning the safety of the product when seeking marketing authorisation in the United States or Europe. A "defect" exists if the safety of the product is not such as persons generally are entitled to expect: 1987 Act, section 3(1). If the manufacturer of a medicine deliberately omits any warning of CV risk which they know of from the SPC, then *prima facie* the safety of the product is not as the consumer is entitled to expect from a consideration of the terms of the SPC.

Discussion and decision

[45] The Lord Ordinary took the view that, as pled, these were relatively simple cases, albeit encumbered with unnecessarily lengthy and detailed averments. He gave short shrift to the defenders' arguments to the effect that the respective cases were irrelevant because of a fundamental lack of specification. We agree with the Lord Ordinary's assessment and we propose to follow his approach when it comes to disposal. Proof of a simple case may of course turn out to be very complicated, but proof is not what we are concerned with at this stage.

[46] The Lord Ordinary described the pursuers' averments as straying from giving notice to pleading evidence. That is an understatement. Other criticisms might be advanced of the pursuers' condescendence, particularly statement 2. However, for present purposes all that need be considered are the defender's complaints of lack of specification, in other words the contention that the pursuers have failed to frame their cases with sufficient clarity and precision to allow the defenders know what they have to respond to.

[47] Despite Ms Shand's protests to the contrary, we do not accept that the defenders can legitimately say that they do not have notice of the case against them. When what is in issue is specification, as is self-evident, what is required will depend on the nature of the case but regard must also be had to the identity of whom the pleadings are primarily addressed: the other party; and what the other party is already aware of and what the other party may be taken readily to understand. We were referred to *Macdonald* v *Glasgow Western Hospitals* and *Hayward* v *Edinburgh Royal Infirmary* 1954 SC 453. These were actions against the boards of management of then fairly recently nationalised hospitals, founding on the alleged negligence of members of the resident medical staff. In *Macdonald* it was a house surgeon who was blamed. The board pleaded that they were not vicarious liable for his fault (then an arguable proposition). One of the points taken was that the pursuer's averments were lacking in specification in respect that full particulars were not given as to the precise terms of the surgeon's contract and the extent of the Board's control over him. Lord President Cooper said this at 465:

> "This objection seems to me to come with an ill grace from a state authority to the representatives of a patient under the state scheme. The plea of lack of specification finds its proper application in a case where a defender does not know the case to be made against him and objects to being taken by surprise at the proof. In this instance the Board and their house surgeon know perfectly well what their contract was and how it operated, and the pursuer cannot know these things except by obtaining

> information from the defenders. I am unimpressed by this objection and am surprised that it was taken."

[48] We do not suppose that the defenders in the present case are necessarily as disingenuous as were the Board of Management of Glasgow Western Hospitals, but in considering Ms Shand's submissions that the defenders have not been given fair notice of the case against them, the identity of the defenders and the nature of the activity with which the actions are concerned, provides the context in which her submissions have to be considered. In the actions before us the defenders are the representatives of the various entities responsible for bringing Celebrex to the market, first in the United States and then in the United Kingdom and the rest of the EU. They are the market authorisation holders in the United Kingdom. They are familiar with the regulatory process and the way in which medicinal products are marketed. Subject to the control of the licensing authority, they are responsible for framing the terms of the relevant SPC and PIL. They may be taken to know all that is known about Celebrex and its effects.

[49] What we have designated as ground of appeal 1 is directed at the sufficiency of specification and therefore the relevancy of the pursuers' common law case whereas what we have designated as ground of appeal 2 is directed at the sufficiency of specification and therefore the relevancy of the pursuers' case based on the Consumer Protection Act 1987. While there is overlap as between the two grounds, ground 1 focuses on inadequate specification of "risk" whereas ground 2 focuses on inadequate specification of "defect". It is convenient to look at "defect" first.

[50] In ground 2.2 the defenders contend that there is, at best, ambiguity as to the defect of which the pursuers are complaining. We see no such ambiguity, although it would have to be conceded that the matter is put more clearly in Mr Jarvie's pleadings than those of

Mr Richards's. As we have already observed, in terms of section 3 of the Consumer Protection Act there is a defect in a product if the safety of the product is not such as persons generally are entitled to expect. In each of the actions the pursuers aver that, as a pharmaceutical product, Celebrex was defective and that not only was it defective but that the defenders knew that to be so. In each of the actions the pursuers go on to make averments about alterations to the warnings on the packaging for Celebrex and in the PIL, concluding that a warning should have been applied from the outset. We would therefore see it as reasonably clear from the Record in either of the actions what it is the pursuers are complaining about, but the point is quite specifically addressed in the pleadings in Mr Jarvie's action to which reference was made in the hearing before us. There, at statement 7 (page 64D) it is stated (emphasis added):

> "Persons consuming Celebrex, including the pursuer, were entitled to expect that it would not carry the high risk of adverse cardiovascular events, such as that which befell the pursuer as hereinafter condescended upon. The pursuer was entitled to expect that Celebrex would not cause or materially contribute to the cardiovascular event suffered [by the pursuer] *without a clear warning being given to that effect*."

[51] Thus, and this was confirmed as the being the position by Mr Smith, the pursuers do not say that there is anything intrinsically defective about Celebrex. What makes it a product that has a defect is that it was marketed without a warning as to the risk of adverse CV events associated with its long-term consumption.

[52] Staying with "defect" but also beginning to address what the grounds of appeal have to say about "risk", at ground of appeal 2.1 the defenders aver that consumers of a medicinal product are not entitled to expect that such a product will be free from risk. They refer to *Wilkes* v *Depuy International Ltd* where, at para 13 of his judgment, Hickenbottom J observed that no medicinal product is free from risk, in the sense of the hazard or chance of the happening of a particular adverse event that will cause loss or damage. That may be so.

However, under the regulatory regime described above, no medical product is marketed without information being given in writing about any relevant risks of adverse effects consequent on the use of the product. The media through which such information is given include SPCs and PILs. Thus, the defenders may be correct when they say that consumers are not entitled to expect that a medicinal product will be free from all risk but, on the other hand, consumers are entitled to expect that where there is a relevant risk which is known about, then it will be the subject of a warning. That proposition is the basis of both the pursuers' common law and statutory cases and we see it to be clearly spelled out in their pleadings. To the extent that ground of appeal 2 depends on a supposed failure to specify what is the "defect" which is founded upon, it must be rejected.

[53] At ground 2.3 the defenders complain that, if it is the pursuers' case that the defect in Celebrex was a deficiency in warning, then the pleadings do not give notice of what that deficiency in warning was. This echoes the complaint at ground 1.3 that the pursuers do not aver by what means and in what terms the defenders had a duty to "bring any known defects, risks, dangers or side effects of the drug to the attention of consumers and medical practitioners."

[54] "Deficiency in warning" is the defenders' expression. We are not aware of it occurring anywhere in the pursuers' pleadings. What the pursuers found on, and in our opinion this is critical to the assessment of the relevancy of their pleadings, is the complete absence of any warning to the licensing authority, to medical practitioners, or to patients of the increased CV risks associated with Celebrex and known about by the defenders. That this is the pursuers' position appears at statement 2.3:

> "The SPC proposed by the defenders [to the Swedish Medical Products Agency] made no reference to increased risk of adverse serious cardiovascular events caused by Celebrex. After marketing authorisation was granted in the UK, the SPC for

> Celebrex 100 mg and 200 mg capsules did not warn of cardiovascular risks associated with the drug. Under the heading 'Undesirable Effects', very rare side effects include 'Cardiovascular: heart failure, myocardial infarction'. These were said to be less than 1 in 10,000 patients, or in isolated reports. ...Celebrex first appeared in the British National Formulary ...in September 2000 ...There was no specific warning about cardiovascular risk."

What the pursuers aver the defenders did not do but should have done appears later in statement 2.3:

> "The defenders ought to have included a warning in the proposed SPC and all later approved versions of the SPC that Celebrex increased the risk of patients suffering serious adverse cardiovascular events."

At statement 2.5 there is this:

> "... no proper warnings were provided that communicated the information on risks that the defenders were in fact aware of. At no time did the warning labels or patient information leaflets disclose the truth, viz that there was a significantly increased CV risk to patients."

The only duty on which the pursuers rely in respect of their negligence case is as follows (statement 6):

> "The defenders had a duty to bring any known, defects, risks, dangers or side effects of the drug to the attention of consumers and medical practitioners prescribing the drug that there was a risk of increased myocardial infarction associated with the long term use of Celebrex"

There follows the averment of breach:

> "They did not do so until after the pursuers had ceased taking the medication."

Causation is addressed in the following sentence:

> "Had the defenders fulfilled the duties incumbent upon them, the pursuer's GP would not have prescribed Celebrex and the pursuer would not have suffered the loss, injury and damage as hereinafter condescended."

[55] As we would see as being quite clear from the pursuers' averments, their case against the defenders is that of an absolute failure to give information about a relevant matter of which the defenders were aware. That is so both in respect of their case of

common law negligence and in respect of their statutory case. Once that is appreciated, any basis that there might otherwise be for grounds of appeal 1.3 and 2.3 falls away. It is enough that the pursuers aver that a warning about a relevant risk which should have been given was not given. As Mr Smith was able to illustrate, there are a number of averments to that effect.

[56] Given that the pursuers' case is that of an absence of warning in the context of a regulatory scheme with which the defenders must be taken to be very familiar, we were particularly unimpressed by the complaints that appear in ground of appeal 1.3 that the pursuers had failed to specify by what means, notification of warnings should have been made, and to whom notification by that means should have been directed. As we have explained above, the SPC is one of the ways in which an applicant for marketing authorisation communicates with the licensing authority and that document, once approved, will be a source of information for the medical profession either directly or indirectly, as will the PIL, which is also available to the individual patient for whom the drug is prescribed. The pursuers specifically aver that the SPC for Celebrex made no reference to the increased risk of CV events caused by the drug. "Prescribing doctors and patients", "GPs, or to patients directly", "the public or GPs" and "the public and GPs" are all identified in the pleadings as those to whom information about the relevant risk should have been communicated.

[57] In this latter part of our opinion we have referred to the risk which, according to the pursuers, gives rise to a duty to warn medical practitioners and their patients, as the "relevant risk". That formulation avoids identifying just what it is that we are talking about. Grounds of Appeal 1.1 and 1.2 present a similar criticism of the pursuers' pleadings. Ms Shand argued that, for all the various formulations which were to be found in the

pursuers' averments, they nowhere identify just what the "risk" associated with Celebrex was. She submitted that it was for the pursuers to identify and with a degree of precision to quantify, the risk of which they said the defenders were aware. This was important in determining what duties such a risk gave rise to. It was also important for the purpose of establishing causation both at the stage of determining what the pursuers and their medical advisers would have done if informed of the particular risk, and at the stage of determining whether the risk which eventuated when the pursuers suffered their respective CV events was the same risk as that of which they should have allegedly been warned (a risk which does not eventuate being irrelevant). This, Ms Shand submitted, was not achieved by references to a number of studies and trials some of which had involved taking Celebrex at dosages in excess of that authorised for therapeutic use in the United Kingdom.

[58] For the purpose of these actions the pursuers define what they mean by the relevant risk at statement 2.6 of condescendence where it is averred:

> "Selective blocking of the COX-2 enzyme interferes with the production and operation of prostacyclin, rendering the formation of blood clots more likely. Prostacyclin acts chiefly to prevent platelet formation and the clumping that is involved in clotting. Increased risk of clots causes an increased risk of stroke or [myocardial infarction]. Patients not at risk previously could become at risk; and those already at risk had an increased risk of an adverse effect. The increase of risk is a material risk, being more than *de minimis*."

In the same statement the pursuers go on to aver that the defenders were aware of this particular risk prior to Celebrex being granted market authorisation in the United Kingdom but that they did not communicate that information to the licensing authority:

> "As is otherwise averred, as from 1999 onwards, the defenders had evidence that Celebrex was implicated in significant and materially increased risk of serious cardiac side effects. The dangers were not disclosed until January 2005."

[59] In our opinion these averments are sufficient for the purpose of the pursuers' case. We return to the point made above. The pursuers allege that the defenders provided simply no information about the increased risk of clot formation and the consequent increased risk of stroke and myocardial infarction associated with the use of Celebrex, either to the licensing authority or to patients and doctors. They allege that the defenders knew about the risk but chose not to disclose it. The pursuers go on to allege that they were prescribed Celebrex and as a result suffered strokes and a myocardial infarction respectively, events which they say were within the scope of the risk (cf *BPE Solicitors* v *Hughes-Holland* [2017] 2 WLR 1029), whereas had they and their medical advisers known of the risk they would not have agreed to prescribe or take the drug. That, as the Lord Ordinary observed, is a relatively simple case. For the purposes of such a case it is sufficient to aver that the deliberately undisclosed risk was "a material risk, being more than *de minimis*."

[60] We would accept that identifying a risk as a "material" risk involves some circularity; a risk is material because it is a risk that should not be ignored. Moreover, proving that a risk is material may become a quite complicated evidential and evaluative exercise. At para 14 of *Wilkes* Hickenbottom J quotes para 13.29 of Powers & Barton. There the authors say this:

> "Determining the safety of a product is a holistic approach that calls for an integrated assessment of the clinical and laboratory adverse effects associated with the product in terms of their frequency, seriousness, severity, reversibility and outcome, and determining whether the risk can be mitigated by warnings on any risk factors. That assessment is complex and takes into account a range of factors including the nature of the disease or condition to be treated, the type of patient and the duration of treatment. It is important to appreciate that regulators approve or disapprove a drug on the basis of risk/benefit at a population level and not at an individual patient level."

However these complexities are matters for proof. The pursuers have committed themselves to the position that the increased risk of an adverse CV event was material, just

as they have committed themselves to the position that no warning of that was given despite it being known to the defenders. The Lord Ordinary was correct to allow the pursuers to attempt to prove that. The various references to studies and trials provide hints as to how they will go about that but, given the nature of the pursuers' case, to require them to go further by way of averment would be to require them to plead evidence (more accurately, more evidence) and argument.

[61] The submissions in relation to grounds 1 and 2 raised a number of incidental points. Ms Shand argued that reference to studies where subjects had been taking in excess of the United Kingdom authorised dose was irrelevant. We disagree. What is to be made of such studies is a matter for determination at proof; the pursuers also make reference to studies where subjects were taking the United Kingdom therapeutic dose. Ms Shand criticised the failure to aver the particular level of risk to which the individual pursuers were exposed. Mr Smith's response was that it is not medically or scientifically possible to define the statistical risk of CV events to all patients from the ingestion of Celebrex on the basis of a single study in terms of a single figure. We suspect that that may be correct, but again it is a matter for proof as to the extent to which it is legitimate to ascribe the experience of a population to the experience of an individual. Ms Shand also submitted that the pursuers do not aver what would have happened if the desiderated warning had been given. As we have perhaps already indicated, we do not accept that. The pursuers' case is that their general practitioners would not have prescribed Celebrex for them. That seems to us clear from the pursuers' averments; that is what they offer to prove.

[62] We accordingly reject grounds of appeal 1 and 2 in their entirety.

[63] Ground of appeal 3 is directed at the averments alleging fraud and deceit on the part of the defenders in failing to disclose information as to the association between the ingestion

of Celebrex and adverse CV events. Ms Shand submitted that these averments were insufficiently specific but if that submission was not accepted they were in any event irrelevant.

[64] We do not question the correctness of Lord Macfadyen's statements of the law in *Royal Bank of Scotland* v *Holmes* and *Buchanan (Stewart) Gauges Ltd* v *BEC (Scotland) Ltd* but in so far as they are applicable in the circumstances of the present cases, we consider that they were correctly applied by the Lord Ordinary when he allowed proof of all but one of the passages in the pursuers' averments which the defenders had criticised as not meeting the rigorous standards for a case of fraud. We say "in so far as they are applicable", because the pursuers' cases do not depend on establishing the delict of fraud as such. What is critical in any case, as the Lord Ordinary appreciated, is that a party is given fair notice of his opponent's position and in assessing that the strictures of Lord President Cooper in *Macdonald* apply. Lord Macfadyen addressed that in *Buchanan* in a passage quoted by the Lord Ordinary in his opinion in the present case:

> "The party against whom any allegation is made is entitled to have fair notice in the other party's pleadings of the substance of the allegation. Where the allegation is of fraud, the courts have applied that rule of fairness particularly strictly. But, in my view, even in a case of fraud, a defender is not entitled to complain of lack of specification if the pursuer's pleadings give him what in the circumstances amounts to fair notice of the allegation. He cannot, through reliance on the authorities about the high standard of specification required in cases of fraud, demand that the pursuer's averments go into more detail than is necessary to give fair notice of the case."

[65] We see the Lord Ordinary as having considered each of the criticised passages of averments from the perspective identified by Lord Macfadyen in *Buchanan* as being appropriate. In all but one instance the Lord Ordinary held the averments to be sufficiently specific. We agree with that assessment for the reasons given.

[66] The defenders submit that these averments are in any event irrelevant. We disagree. The pursuers' case is that the CV risks associated with Celebrex were known to the defenders and that as applicants for marketing authorisation and then suppliers of the product to the public they were under a duty to disclose that information. In the absence of a warning of these risks it is contended that Celebrex is a product with a defect for the purposes of the Consumer Protection Act. It may not be necessary for the pursuers to succeed in that case that they prove fraud on the part of the defenders, but it cannot be said to be irrelevant to their case, namely that the defenders knowingly omitted data or information concerning the safety of the product when seeking marketing authorisation in the United States or Europe and in their subsequent interactions (or absence of interactions) with the regulatory authorities or that they made false claims as to the safety of Celebrex or that they selectively released data or that they otherwise kept information from the public. Evidence that the defenders deliberately chose not to disclose information and the available inference that this was done so as not to impact adversely on the marketability of the product, would clearly be relevant to inform the question as to what persons generally are entitled to expect for the purpose of section 3 of the 1987 Act and to displace any suggestion of there being a defence in terms of section 4 (1) (e) that the state of knowledge was not such that a producer of such products might be able to discover the defects. Moreover, if, as Ms Shand argued, regulatory approval is powerful evidence that the level of safety which people were entitled to expect had been achieved, evidence that approval had been given as a result of fraud would be relevant to displace the significance of the regulatory authority having given marketing authorisation.

[67] We accordingly reject ground 3.

[68] We shall refuse each of the reclaiming motions. We reserve all questions of expenses.

Postscript

[69] As the Lord Ordinary decided, these actions can now proceed to proof. It is not however too late for more active case management than has apparently proved possible so far. We have insufficient information to determine the reasons for this but on the face of it only limited progress has been made despite these actions being raised some eight years ago. There may be difficulties of which we are not aware, but if that is so then parties and the court should set about addressing them.

Appendix

Acronym	**Full name**
CHM	Commission on Human Medicines
CHMP	Committee for Medicinal Products for Human Use
COX-1	cyclo-oxygenase 1
COX-2	cyclo-oxygenase 2
CPMP	Committee for Proprietary Medicinal Products
CSM	Committee on Safety of Medicines
CV	Cardiovascular
EMA	European Medicines Agency
EMEA	European Agency for the Evaluation of Medicinal Products
FDA	United States Food and Drug Administration
MCA	Medicines Control Agency
MHRA	Medicines and Healthcare Products Regulatory Agency
NSAID	Non-steroidal Anti-inflammatory Drug
PIL	Patient Information Leaflet

SPC or SmPC	Summary of Product Characteristics