ACMD

Advisory Council on the Misuse of Drugs

Annex for the ACMD Anabolic Steroids Report, A-F;

September 2010

Annex A – ACMD Membership

Current members of the Advisory Council on the Misuse of Drugs (ACMD)

Member	Sector
Professor Leslie Iversen (ACMD Chair)	Professor of Pharmacology, Oxford University
Dr Dima Abdulrahim	Briefings Manager, National Treatment Association
Lord Victor Adebowale	Chief Executive, Turning Point
Dr Jason Aldiss	Veterinary Medicine and Public Health - Managing Director of Eville & Jones Ltd
Mrs Gillian Arr-Jones	Chief Pharmacist for the Care Quality Commission
Mr Martin Barnes	Chief Executive, Drugscope
Dr Margaret Birtwistle	Specialist General Practitioner, Senior Tutor – Education and Training Unit, St George's Hospital and Forensic Medical Examiner
Commander Simon Bray	Commander, Metropolitan Police
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Ms Carmel Clancy	Principal Lecturer for Mental Health and Addiction, Middlesex University
Professor Ilana Crome	Professor of Addiction Psychiatry, Keele University
Ms Robyn Doran	Mental Health Nurse and Director of Operations, North-West London Mental Health Trust
Professor Simon Gibbons	Professor of Phytochemistry (natural product chemistry), School of Pharmacy, University of London
Mr Patrick Hargreaves	Advisor for Drugs and Alcohol, Durham County Council Education Department
Ms Caroline Healy	Children's Strategic Adviser
Professor Raymond Hill	Professor of Pharmacology, Imperial College London
Mr David Liddell	Director, Scottish Drugs Forum

Mr Hew Mathewson CBE	Dentist and former President and Chair of the General Dental Council (2002 to 2009)
Dr Fiona Measham	Senior Lecturer in Criminology, University of Lancaster
Mr Graham Parsons	Pharmacist
Mr Trevor Pearce	Director of Enforcement, Serious Organised Crime Agency
District Judge Justin Phillips	District Judge, Drugs Court London
Mr Richard Phillips	Independent Consultant,
DCC Howard Roberts	Former Deputy Chief Constable, Nottinghamshire Police
Dr Mary Rowlands	Consultant Psychiatrist in Substance Misuse, Exeter
Ms Monique Tomlinson	Freelance Consultant in Drugs Misuse
Mr Arthur Wing	Director, Surrey & Sussex Probation Trust

Annex B – Additional Expertise

Lucy Blackburn	Department for Culture, Media and Sport
Dr Rob Dawson	General Practitioner
Patrick Deller	HM Customs and Excise
Michael Evans-Brown	Liverpool John Moores University
Noel Gill	Public Health Laboratory Service
Roy Jones	Turning Point
Dr Les King	Former Head of Drugs Intelligence Unit, Forensic Science Service
Dr Andrew Kicman	King's College London
Dr Pirkko Korkia	University of Bedfordshire
Jim McVeigh	Liverpool John Moores University
Professor Geoff Phillips	Retired Chemist
Ric Treble	Government Laboratory Chemist
Marion Walker	Pharmacist, Berkshire Healthcare NHS Foundation Trust
Dr Mike White	Forensic Science Service

Departmental Representation

David Carter	Medicines and Healthcare products Regulatory Agency
Mark Prunty	Department of Health
Lynda Scammell	Medicines and Healthcare products Regulatory Agency
Angela Scrutton	Home Office

Annex C. Pharmacology and Chemistry

Within the UK, there are few currently licensed preparations containing anabolic steroids. Testosterone and mesterolone are available for male hypogonadism (where patients fail to produce sufficient testosterone). Nandrolone is licensed for osteoporosis but it is not recommended as a therapeutic agent for this purpose. Oxymethelone is also available on a named patient basis for the treatment of aplastic anaemia. Other anabolic steroids continue to be available as pharmaceutical preparations in many countries,and are relatively easy to obtain for non-medicinal purposes.

Anabolic steroids are supplied as tablets or capsules for swallowing (oral administration) and in vials for injection (intramuscular administration). Testosterone preparations are also available for administration through the skin (transdermal), within the mouth itself (sublingual or buccal routes), or by implantation into the abdomen (as well as testosterone formulations for oral administration or intramuscular injection).

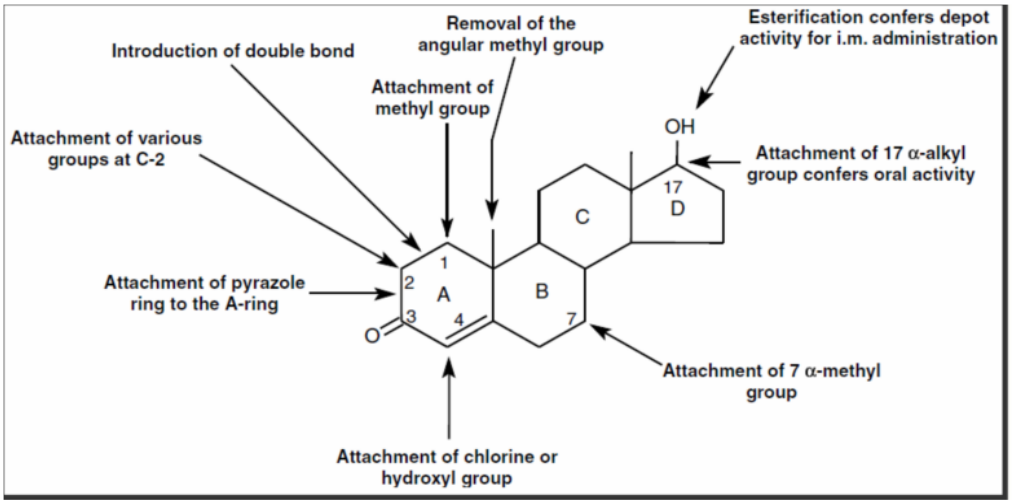
Non-pharmaceutical preparations of anabolic steroids are additionally available, marketed for body building purposes. These are not necessarily produced in accordance with Good Manufacturing Practice. Non-pharmaceutical water-based testosterone suspensions for injection into a muscle have been advertised and discussed on bodybuilding web sites. The testosterone will rapidly enter the systemic circulation following administration, as it is present in an aqueous rather than an oily injection vehicle. A relatively recent phenomenon is the availability of novel anabolic steroids sold as dietary supplements, which arose initially as 'prohormones,' as a consequence of the Dietary Supplements Health and Education Act passed by US Congress in 1994. Steroidal 'dietary supplements' were originally supplied in capsules as prohormones, so-called because, following their oral administration; they are converted within the body to the potent hormones testosterone or nandrolone (and also to a relatively large proportion of inactive metabolites for excretion). These prohormones are androstenedione, androstenediol and their corresponding 19-nor analogues. In 2004, the USA Anabolic Steroid Control Act included isomers of androstenediol and androstenedione, and their 19-nor analogues amongst the list of anabolic steroids (but not dehydroepiandrosterone; DHEA). As a consequence, the availability of these prohormones appears to have dropped remarkably, judging by the decrease in the number of advertisements for these compounds on the Internet.

This is of little consequence, as the steroidal dietary market had rapidly evolved in that time to the supply of analogues of existing anabolic steroids and those that were never commercialised, many appearing to originate from China. Such steroids are sometimes now referred to as 'Designer Steroids'. They have been marketed, presumably, as they can be exempt from existing statutory controls regarding the manufacture and supply of drugs and further not to violate existing patents. They are advertised on many bodybuilding web sites. Examples include prostanozolol and 1-testosterone. Some analogues also appear to rely on metabolism, following their administration, to activate

the compound, for example, desoxymethyltestosterone and 6-methylandrostenedione.

There is a concern that some athletes will also use these supplements, necessitating sports anti-doping accredited laboratories to expand their drug screens on a continuous basis. These steroids are not to be confused with the very few anabolic steroids that have been specifically supplied in an attempt to circumvent sports drug tests, such as tetrahydrogestrinone (THG). The efficacy of these designer steroids/dietary supplements is not proven and they have not undergone drug safety tests, as must be performed rigorously in the pharmaceutical industry. It is unlikely that such products have any adverse effects that have not already been described in the literature regarding anabolic steroid administration. It is possible, nonetheless, that eventually an analogue will be produced that will cause unexpected toxicity of an acute and severe nature to humans.

Figure 1- With respect to the structure of testosterone, some of the chemical modifications that have been introduced in an attempt to maximise the anabolic effects relative to the androgenic effects.



Chemistry and Pharmaceutical Preparations

Oral activity of anabolic steroids can be conferred by substitution of the 17-alpha hydrogen, which can be replaced with an alkyl group, either methyl (-CH_3) or ethyl (-C_2H_5), thus making the 17-alkylated anabolic steroids such as for example, methyltestosterone, methandienone, norethandrolone and stanozolol. Absorption occurs across the gut into the hepatic-portal vein, and thus to the liver, where compounds are converted into more water-soluble products for excretion. The presence of the alkyl function hinders this conversion process, allowing such steroids to remain biologically active and, thus, they continue to flow intact through the liver, entering into the systemic circulation. A methyl group attached to C-1 can also confer oral activity, as in methenolone or mesterolone.

Injectable preparations do not require a 17-alkyl group as they are administered into a muscle, so the steroid is then released directly into the systemic circulation, rather than first passing through the liver. To permit slow

release of the steroid from the injection site, the steroid is administered in an oily liquid. Usually, the hydroxyl group (-OH) on the D-ring of anabolic steroid has also been bonded to an acid moiety to form an 'ester' linkage, giving even better retention within the oil. These esterified steroids are thereby slowly released into the blood circulation, where esterases cleave the bond to yield the biologically active anabolic steroid. The esters include cyclohexylpropionate, decanoate, laurate and phenylpropionate for nandrolone; acetate, cypionate, decanoate, enanthate, isocaproate, phenylpropionate, propionate and undecanoate for testosterone, undecylenate for boldenone and acetate for trenbolone. The mechanism of action of esterified nandrolone and other anabolic steroids, and the effect of drug delivery systems on their biological activity have been studied by van der Vies, 1993[1]. The duration of action of the esters depends upon the rate of absorption from the site of administration. This is dependent on the chain length of the acid moiety and also the formulation, being related to the partition coefficient of the derivatives between the oil used in the formulation and plasma. In general, the longer the chain length, the more slowly the preparation is released into circulation, thus prolonging the duration of action.

Conversion of Weaker Androgens to Testosterone

A minor amount of testosterone is derived from the body biochemically converting weaker androgens secreted by the testis, ovary and adrenal cortex. These weaker androgens are secreted into the systemic circulation and then subsequently converted to testosterone by other organs and tissues by the process of metabolism. The weaker androgens, dehydroepiandrosterone (DHEA) and androstenedione are not only converted peripherally to testosterone but also to the even more potent androgen 5-alpha-dihydrotestosterone, often referred to simply as dihydrotestosterone or DHT. As a consequence of the relatively small amount of testosterone produced, the peripheral metabolism of weaker androgens to testosterone has much greater relevance in the female than in the male (Kicman, in press; Longcope, 1986).

Effects on Hair Follicles

An obvious effect of androgens in the female is at puberty, where the soft (vellus) hair in the skin of the pubic region and also in the armpits is targeted, being converted to the coarse (terminal) hair. In boys at puberty, terminal hair is also produced on the face, called beard hair follicles ('whiskers'). In other regions such hair growth depends on a number of factors, such as race, sex, age, and the site of the follicles (Brooks, 1984). The development of beard hair follicles is one of the secondary sexual characteristics which are manifested during puberty in boys. Other androgenic effects include the enlargement of the larynx causing a deepening of the voice, an increase in sebaceous gland activity and central nervous system (CNS) effects (increased libido and aggression). Anabolic effects are the growth of skeletal muscle and bone; the stimulation of linear growth eventually ceasing due to the closure of the epiphyses. Women exposed to unnaturally large amounts of

[1] van der Vies, J. (1993). Pharmacokinetics of anabolic steroids. Wiener medizinische Wochenschrift,1993,143(14–15), 366–368.

androgens, such as by the chronic use of anabolic steroids, will become hirsute and eventually undergo virilization (the appearance of the male secondary sexual characteristics in the female). The development of beard follicles and the deepening of the voice are considered to be largely irreversible.

Medical Applications

The potential of anabolic steroids as therapeutic agents to increase weight, lean body mass and strength is being revisited. Anabolic steroids may play a significant role in the treatment of cachexia (wasting of muscle, loss of weight and appetite) associated with HIV/AIDS, severe burns and renal failure, where nutrition and standard care have been ineffective (Basaria *et al*., 2001). Carefully designed clinical trials may eventually give the definitive answers as to the usefulness of anabolic steroids as medicines, and whether xenobiotic anabolic steroids offer any advantage over very large (supraphysiological) doses of testosterone to men. In the interim, it seems sensible to consider hormone replacement therapy to men in a catabolic state, where there is a significant decrease in circulating testosterone associated with certain chronic diseases (severe burn injuries or HIV/AIDS-associated wasting).

Mode of Action

Anabolic steroids are thought to exert their actions by several different mechanisms (Kicman, 2008). These mechanisms include modulating androgen receptor expression as a consequence of (i) directly affecting the topology (shape) of the androgen receptor and thus subsequent interaction with comodulators (mainly coactivators) and transcriptional activity and (ii) intra-cellular metabolism. Other mechanisms include (iii) an 'anticatabolic' effect by interfering with glucocorticoid receptor expression; and (iv) by non-genomic, as well as by genomic pathways, in the brain resulting in behavioural changes.

Once an androgen docks to an androgen receptor in a cell, the receptor changes its shape into an 'active' conformation where it can then link to a specific site on DNA within a cell. In fact, two receptors can bind to this site, referred to as a homodimer, which amplifies the subsequent effect on the DNA. Other proteins called coregulators then cluster around the receptors that are interacting with the DNA site (Heemers *et al*., 2007). This result in gene activation and a resultant alteration in cell function, growth or differentiation.

It is assumed that anabolic steroids with enhanced anabolic activity, for example nandrolone, oxandrolone and stanozolol, alter the shape of the active androgen receptor in a somewhat different way compared from that if testosterone had bound to the receptor (Feldkoren *et al*., 2005; Holterhus *et al*., 2002). The active receptors still bind to the DNA but there is a different interaction with the coregulators, thus affecting gene activation in a way that may enhance, or in some cases, suppress gene activation. An appealing hypothesis is that anabolic-androgenic dissociation can also occur due to interaction with various coregulators in different tissues; thus growth in muscle is stimulated as a result of interaction with particular coregulators but in

androgenic target tissues the interaction is with different coregulators to those in muscle. There is little data, as yet, to support such a hypothesis, but it is known that the androgen coactivator FHL2 is expressed predominantly in the myocardium of the heart and the epithelial cells of the prostate (Muller *et al*., 2000), and a number of other androgen receptor coregulators appear to be enriched in certain tissues (Heemers and Tindall, 2007) [2]. How an anabolic steroid may affect androgen receptor conformation and interaction with particular coregulators is of obvious interest, as such knowledge may eventually offer an additional mechanism for anabolic-androgenic dissociation. Anabolic-androgenic dissociation may also occur due to intracellular metabolism. For example, in several androgenic target tissues, testosterone is converted to DHT, which binds more strongly to the androgen receptor but, by contrast, the anabolic steroid nandrolone is converted to a product that binds more weakly to this receptor (Celotti *et a*l., 1992; Toth *et al*., 1982). This conversion does not significantly occur in human skeletal muscle, as in this tissue there is a lack of a converting protein (enzyme) called 5-alpha-reductase (Thigpen *et al*., 1993). Hence, in muscle, nandrolone retains a stimulating effect but in androgenic tissues its effect is weakened, for example, permitting more 'muscle per whisker'.

It is possible, but remains to be proven, that anabolic steroids may also interfere with the action of glucocorticoids. One action of glucocorticoids is to stimulate breakdown of protein in skeletal muscle for the production of glucose, principally this being due to a glucocorticoid called cortisol. Cortisol is produced naturally in the body and its production increases considerably when the body is physiologically stressed. Anabolic steroids may counteract the catabolic effect by interfering with glucocorticoid receptor expression at the gene level but this remains unproven (Hickson *et al*., 1990).

The endocrinology of skeletal muscle is highly complex and there is a delicate balance between synthesis and breakdown during growth, health, disease and ageing (Sheffield-Moore *et al*., 2004). It is this complexity that makes it challenging to resolve the significance of anabolic steroids as anabolic (and anti-catabolic) agents across the spectrum, from the healthy athlete who desires faster recovery from arduous training schedules where cortisol may be somewhat raised to the patient with severe physical trauma, such as from a burn injury, where there is extreme hypercortisolaemia (very raised circulating cortisol) and hypoandrogaenemia (lowered circulating androgens).

The behavioural effects of androgens/anabolic steroids inmen and women include those concerning sexual behaviour, cognitive abilities, aggression and mood Androgen receptors mediate the effects of anabolic steroids in the mammalian brain; the expression of progestogen and oestrogen receptors may also be affected. Non-genomic pathways are important too, i.e. cellular pathways not involving the androgen receptor binding to DNA. Induction of aggression in animals, by administering anabolic steroids, appears to overlap with neural circuits underlying the regulation of aggression by endogenous

[2] Heemers HV, Tindall DJ. Androgen receptor (AR) coregulators: A diversity of functions converging on and regulating the AR transcriptional complex. Endocrine Reviews 2007; 28:778-808.

androgens, these being systems utilising the substances GABA, serotonin and arginine vasopressin (Clark *et al*., 2003).

Annex D. Contamination of Medicinal Products and Dietary Supplements with Anabolic Steroids

Some products have been contaminated with APIs (Active Pharmaceutical Ingredients) such as anabolic steroids (e.g. methandienone and stanozolol) (Baume *et al*., 2006; Geyer *et al*., 2003; Geyer *et al*., 2008; Parr *et al*., 2007), centrally acting appetite suppressants (e.g. sibutramine and rimonabant) (Food and Drug Administration, n.d.a, Jung *et al*., 2006), diuretics (e.g. bumetanide and furosemide) (Food and Drug Administration, n.d.a; Food and Drug Administration n.d.b; Hoggan *et al*., 2007) and drugs for erectile dysfunction (e.g. tadalafil) (Medicines and Healthcare products Regulatory Agency, 2009). Products have also been openly, albeit unlawfully, marketed as containing clenbuterol (Parr *et al*., 2008) (a β2 agonist) and dinitrophenol (an uncoupler of mitochondrial oxidative phosphorylation (Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment, 2003)). Moreover, some of these APIs were found to be present at high strength (Baume *et al*., 2006; Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment, 2003; Geyer *et al*., 2003; Geyer *et al*., 2008; Hoggan *et al*., 2007; Jung *et al*., 2006; Parr *et al*., 2007; Parr *et al*., 2008) (not all reports provided data on this parameter).

Annex E. Harmful effects of anabolic steroids

Background

While the use of anabolic steroids has been associated (Alghabban, 2004; Porta, 2008) with a number of adverse effects on health this area remains poorly researched. Much of the data are derived from case reports/series and cross-sectional study designs that are observational in nature. Observational designs are likely to remain the mainstay for some time, due, in part, to the methodological, ethical and logistical constraints which preclude the use of randomised controlled trials (RCTs) that make use of the high-dose polydrug regimens common to this user group (Evans-Brown & McVeigh, 2009). Many of the studies completed to-date suffer from issues in relation to their design, execution and analysis leading to problems with internal validity and generalisability. This is compounded by the fact that many studies do not provide sufficient detail of the study design to allow a detailed analysis, and, subsequently, comparison across different studies. Issues identified include bias (notably selection bias and information bias) and confounding (Delgado-Rodríguez & Llorca, 2004; Elwood, 2007; Higgins & Altman, 2008; Jenicek, 1999; von Elm *et al*., 2007; Reeves *et al*., 2008; Rothman *et al*., 2008; Sackett, 1979; Vandenbroucke *et al*., 2007). Specifically:

i. A failure to systematically perform drug testing and analysis as part of the study and an over-reliance on self-reported drug use. There has been a failure to recognise the heterogeneous nature of this group including potential confounders.

ii. Inadequate recognition of the compound-specific effects of the drugs, including the degree to which they diverge from the effects mediated by endogenous testosterone. This issue is further compounded by the varied polydrug regimens employed by users and the subsequent failure to systematically record the drugs used, doses taken and duration of use.

iii. The failure to examine in detail whether adverse events (particularly those documented as case reports) are causally associated with use of these drugs (Alghabban, 2004; Porta, 2008).

iv. Many of the adverse effects are subjective self-reports by users which is likely to result in bias: notably sampling bias and information bias (e.g. recall bias). Data are seldom available on the validity of the measures used, with many studies measuring ‘soft’ data variables, including physical and psychological health through simple ‘tick-boxes’ rather than using validated scales and measurements.

v. The failure to take into account/examine the phenomenon of expectancy and placebo effects (Beedie *et al*., 2009; Benedetti, 2009; Kienle & Kiene, 1997; Moerman, 2002).

vi. An over-reliance on case reports as evidence of the incidence of adverse effects and as causal relationships. Case reports are, rightly, the “first line of evidence” (Jenicek, 1999) and “highly sensitive in picking up novelty in a

qualitative way" however, they are "poorly specific as to quantitative confirmation" (Vandenbroucke, 1999). In this group the prevalence of use and extent of exposure is difficult to determine, making any inferences on incidence rates unlikely. Moreover, we are not aware of any reports that have compared these cases to the background incidence in the general population.

vii. A lack of adequately powered prospective cohort studies within this population.

Cardiovascular
While there have been case reports of adverse effects on the cardiovascular system which the authors attribute to the use of anabolic steroids (e.g. Alhadad *et al*., 2010; Bispo *et al*., 2009; Clark & Schofield, 2005; Fisher *et al*., 1996; McCarthy *et al*., 2000; Wysoczanski *et al*., 2008), many of these are inadequately reported and have failed to report potential confounding factors.

Hypertension
The data on anabolic steroid use and hypertension are conflicting. While some cross sectional studies have reported significant increases in blood pressure in those using anabolic steroids (Cohen *et al*., 1988; Lenders *et al*., 1988; Kuipers *et al*., 1991; Grace *et al*., 2003; Urhausen *et al*., 2004), other studies have reported no increase (Hartgens *et al*., 1996; Hervey *et al*., 1976; Riebe *et al*., 1992; Sader *et al*., 2001; Lane *et al*., 2006; Krieg *et al*., 2007; Urhausen *et al*., 1989; Karila *et al*., 2003). Further, some of the studies that reported significant increases in blood pressure found that mean blood pressure was below (Lenders *et al*., 1988; Grace *et al*., 2003) that defined as hypertension (Beevers *et al*., 2007; National Institute for Health and Clinical Excellence, 2006). Freed & Banks (1975) found a significant increase in systolic blood pressure in a cross-over trial using a single oral anabolic steroid (methandienone); Hartgens *et al*., (2003) in a prospective study found no significant increase in blood pressure as compared to non-using controls either at baseline or after 8 weeks of using high-dose self-directed regimens. Differences in the study design, participants and drug regimens could account for these findings.

While self-reported 'high blood pressure' is a relatively common finding in questionnaire-based studies e.g. 33.6% (n=110) (Korkia & Stimson, 1993), 36.4% (n=386) (Lenehan *et al*., 1996) these are subjective measures. A diagnosis of hypertension is not made subjectively (National Institute for Health and Clinical Excellence, 2006).

Lipid metabolism
Data from cross-sectional studies have typically found that high density lipoprotein (HDL) is significantly decreased during anabolic steroid use (Ebenbichler *et al*., 2001; Lane *et al*., 2006; Sader *et al*., 2001). This is supported by a prospective study (Hartgens *et al*., 2004) and data from clinical trials using lower doses of injectable testosterone esters (Singh *et al*., 2002). The effects appear to be dependent on the type(s) of anabolic steroid, dose, duration of use and route of administration (Bhasin *et al*., 1996; Singh *et*

al., 2002). Moreover, it appears that some oral 17α-alkylated steroids have greater effects on reducing HDL than injectable testosterone ester products (Friedl *et al*., 1990; Thompson *et al*., 1989).

The data on anabolic steroid use and low-density lipoprotein (LDL) are conflicting. Although some cross-sectional studies have found a significant increase in LDL in anabolic steroid users (Glazer, 1991), this is not a consistent finding (Ebenbichler *et al*., 2001; Lane *et al*., 2006; Sader *et al*., 2001). Clinical trials using 600 mg/week of injectable testosterone enantate have not found this effect (Singh *et al*., 2006). Again these effects appear to be dependent on the type(s) of anabolic steroid, dose, duration of use and route of administration.

In a prospective study Hartgens *et al*., (2004) found an apparently beneficial significant decrease in lipoprotein (a) (which is an independent risk factor for cardiovascular disease). However this effect was only found in those using high-dose polydrug regimens. In cross-sectional studies Cohen *et al*., (1996) reported a significant decrease in lipoprotein (a) while Palatini *et al*., (1996) reported no significant difference compared to controls.

Overall it appears that lipid metabolism normalises after drug cessation, although the length of time this takes appears to vary and be dependent on drugs used, doses taken and duration of use (Hartgens *et al*., 2004). Further research is required to gain a better understanding of the effects of anabolic steroids on lipid metabolism in users.

Cardiac structure & function

Some cross-sectional studies have found no differences between anabolic steroid users and non-using controls in measured parameters
Salke *et al*., 1985; Thompson *et al*., 1992); while others have observed some significant differences (Climstein *et al*., 2003; Dickerman *et al*., 1997; Karila *et al*., 2003; Urhausen *et al*., 1989; Yeater *et al*., 1996) such as increased left ventricular mass (Karila *et al*., 2003). While some prospective studies have found no differences in measured parameters (Hartgens *et al*., 2003, Palatini *et al*., 1996; Spataro *et al*., 1992; Zuliani *et al*., 1989), others have reported some significant differences (e.g. Piccoli *et al*., 1991; Sachtleben *et al*., (1993). Currently the data available are equivocal. Differences in the study design, methods, participants and drug regimens could account for these findings.

Vascular structure & function

There are limited data on vascular structure and function in steroid users. The data that are available from cross-sectional studies is conflicting. Sader *et al*., (2001) found that while 'high-level' bodybuilding is associated with impaired vascular reactivity and increased arterial thickening, the use of [anabolic steroids] per se is not associated with significant abnormalities of arterial structure or function" (including endothelial dysfunction). Lane *et al*., (2006), however, found that while endothelial-dependent dilation was not impaired compared to controls, endothelial-independent dilation was significantly impaired. Conversely, Ebenbichler *et al*., (2001) found that endothelial-

dependent dilation (indicating endothelial dysfunction) was significantly impaired compared to controls, where as endothelial-independent dilation was not. Differences in the study design, methods, participants and drug regimens could account for these findings.

Insulin resistance
There are limited data on the effects of anabolic steroids on insulin resistance. The data that are available from cross-sectional studies is conflicting. Lane *et al*., (2006) in a cross-sectional study of anabolic steroid users found no change in blood glucose or insulin levels. Cohen & Hickman (1987) found in their cross-sectional study that powerlifters using steroids had a diminished glucose tolerance which they believed to be secondary to insulin resistance, although according to the authors this did not meet the criteria for impaired glucose tolerance according to current guidelines. Singh *et al*., (2002) in a double-blind randomised controlled trial in healthy young men which administered a replacement dose of 600 mg/week of testosterone enantate over 20 weeks found no change in insulin resistance.

Other cardiovascular markers
There are limited data on the effects of anabolic steroids on other markers associated with cardiovascular dysfunction. The data that are available from cross-sectional studies is conflicting.

Ebenbichler *et al*., (2001) and Graham *et al*., (2006) measured homocysteine levels in a cross-sectional study of steroid users. Although plasma homocysteine was found to be significantly increased compared to non-users these were within the reference interval (Antoniades *et al*., 2009; Refsum *et al*., 2004). Interestingly in the Graham *et al*., study (2006), those abstinent from steroid use for the past three months also had significantly higher homocysteine levels compared to bodybuilding and sedentary controls that reported never using anabolic steroids, these were also within the reference interval. Neither study reported adequate details on potential confounding factors that are known to affect homocysteine levels (Refsum *et al*., 2004). Zmuda *et al*., (1997) found no significant increase in plasma homocysteine levels in weightlifters treated with [a low dose] 200 mg/week of testosterone enantate for 3 weeks.

In a double-blind randomised controlled trial in healthy young men which administered a replacement dose of 600 mg/week of testosterone enantate for 20 weeks, Singh *et al*., (2002) found no significant changes in C-reactive protein (a marker of inflammation) compared to those participants receiving lower doses of testosterone.Overall, differences in the study design, methods, participants and drug regimens could account for these findings.

Haemostatic system
There are limited data on the effects of anabolic steroids on the haemostatic system. Lane *et al*., (2006) in a cross-sectional study found no statistically significant differences in prothrombotic factors (of those measured) compared to users who had abstained for three months, bodybuilders who denied current/prior use of anabolic steroids, and healthy sedentary controls.

Alén (1985) and Baker *et al*., (2006) have reported significant increases in haematocrit, compared to controls, in cross-sectional studies of steroid users; 51% and 55.7% respectively (the reference interval is 45–52% for males). The haematocrit levels in the study by Baker *et al*., (2006) were significantly increased compared to sedentary controls and bodybuilders who reported never using anabolic steroids. They were not significantly different from those who had reported abstinence from steroid use in the past three months.

Data from controlled clinical trials of testosterone enantate 600 mg/week have found that there is a dose-dependent stimulatory effect on erythropoiesis and concomitant increase in haemoglobin and haematocrit in both young (19–35 years) and older healthy males (60–75 years). However, the effect was more pronounced in older men and a haematocrit above 54% was not seen in the younger group (Coviello *et al*., 2008). While data are limited it is interesting to note that the mean age of the steroid users in the study by Baker *et al*., (2006) was 42.4±3.8 years and all reported using "various doses [of anabolic steroids] in cyclical fashion over the previous 20 years". Differences in the study design, methods, participants and drug regimens could account for these findings.

Musculoskeletal

There have been several case reports of damage to tendons/ligaments that the authors attribute to the use of anabolic steroid use. It is thought that this could be as a result of disproportionate growth of the muscle compared to the tendons/ligaments. There have also been case reports of rhabdomyolysis (breakdown of muscle) attributed to anabolic steroid use (Braseth *et al*., 2001; Daniels *et al*., 2006; Farkash, 2009), although potential confounding factors have not been sufficiently examined.

Hepatic

The use of some types of anabolic steroids, in particular the 17α-alkylated compounds, has been associated with hepatic dysfunction and disease in clinical populations (Foss & Simpson, 1959; Velazquez & Alter, 2004). While cross-sectional data on liver function appears to demonstrate that liver function can be impaired in some users, the extent of this has been questioned by Dickerman *et al*., (1999) who have suggested that many studies have failed to examine specific markers of liver function and hence could not distinguish between markers of hepatotoxicity and those of muscle damage secondary to high-levels of resistance exercise. Studies have not examined the effect of polydrug regimens used by this group, nor potential confounding factors. Prospective studies that examine specific markers of hepatic function in users are required. There have been a small number of case reports of benign liver tumours (Schumacher *et al*., 1999; Socas *et al*., 2005; Velazquez & Alter, 2004), peliosis hepatis (Cabasso, 1994), and hepatocellular carcinoma (Gorayski *et al*., 2008; Velazquez & Alter, 2004) in anabolic steroid users.

Endocrine & Genitourinary

Data from cross-sectional studies have found that self-reported gynaecomastia is relatively common (Lenehan *et al*., 1996). However, the measures used have not been validated. Gynaecomastia is the growth of the glandular breast tissue in males thought to be caused by an imbalance in the ratio of free oestrogen to testosterone (Braunstein, 2007; Eckman & Dobs, 2008). Estimates of prevalence in the general population range from 60% in pubertal boys, 19% in those aged 16–20, 33–41% in those aged 25–45 and 55–60% in those aged >50 years (Eckman & Dobs, 2008). In anabolic steroid users it is thought to be mediated through the increased peripheral aromatization of exogenous steroids to oestrogenic metabolites and/or alterations in the transport/binding of endogenous oestrogen and testosterone in the blood (Pugeat *et al*., 1981). However, many of the drugs commonly used by this group (such as growth hormone, gonadotrophin, spironolactone) have also been associated with gynaecomastia (Braunstein, 2007; Eckman & Dobs, 2008). The [self-directed] use of selective oestrogen receptor modulators (particularly tamoxifen) (Lenehan *et al*., 1996; Baker *et al*., 2006), and, increasingly, aromatase inhibitors (Cohen *et al*., 2007; Parkinson & Evans, 2006) that are taken as both prophylactics to, and, for the treatment of, gynaecomastia is relatively common in this group.

Data from clinical trials have demonstrated that high levels of exogenous anabolic steroids can suppress endogenous testosterone production and spermatogenesis, although there is considerable variation in this effect depending, inter alia, on the type of steroid used (Grimes *et al*., 2007). This effect is currently being tested in clinical research for the use of testosterone esters as a male contraceptive (Grimes *et al*., 2007). What is believe to be a similar effect has been reported in case reports/series and cross-sectional studies of steroid users, being associated with transient testicular atrophy and infertility (Boyadjiev *et al*., 2000; Drakeley *et al*., 2004; Gazvani *et al*., 1997; Jarow *et al*., 1990; Karila *et al*., 2004; Knuth *et al*., 1989; Lloyd *et al*., 1996; Menon, 2003; Moretti *et al*., 2007; Peña *et al*., 2003; Ritter *et al*., 2005; Turek *et al*., 1995). For some individuals it appears that it can take many months for endogenous testosterone production and fertility to recover (Gazvani *et al*., 1997).

It is common for users to self-report increased libido during an “on” cycle (i.e. when using anabolic steroids). Conversely, during an “off” cycle users often report that libido is reduced (Bolding *et al*., 2002; Korkia & Stimson, 1993; Korkia *et al*., 1996; Lenehan *et al*, 1996; Grace *et al*., 2001; Midgley *et al*., 2000). Some report no changes in libido. The measures used have not been validated. Moss *et al*., (1993) reported that current anabolic steroid users reported significantly more sexual intercourse compared to former users and non-users. However, the majority of users in this study were using what would be regarded as low doses of anabolic steroids. Further, the composition (inc. dose) of the drugs were not quantified. Interestingly, in a clinical trial that used a replacement dose of 600 mg/week of testosterone enantate for 20 weeks there were no changes in self-reported sexual activity and sexual desire (Sinha-Hikim *et al*., 2002).

It is possible that the reported reduced libido could be due to the suppression of endogenous testosterone production (anabolic steroid-induced hypogonadism) when ceasing use (although there is limited data on testosterone levels in users when ceasing a cycle). Users have self-reported erectile dysfunction both during “on” cycles and “off” cycles. Overall, this area of research has received little attention (Moss *et al*., 1993). It is relatively common that individuals report the use of human chorionic gonadotropin (Lenehan *et al*., 1996; Baker *et al*., 2006) that is taken as both prophylactics to, and, for the treatment of, anabolic steroid-induced hypogonadism.

Little data exists on the sexual health of this group. However, this issue (along with blood-borne virus transmission) needs to be viewed within the wider public health concerns of spread of sexually transmitted infections.

We are aware of two case reports of prostate cancer in steroid users (Larkin, 1991; Roberts & Essenhigh, 1986); two cases of renal cell carcinoma (Bryden *et al*, 1995; Martorana *et al*., 1999); and, one of Wilms’ tumor (Prat *et al*., 1977).

Dermatological & Hair

In cross-sectional studies, large numbers of steroid users self-report acne (Bolding *et al*., 2002; Korkia & Stimson, 1993; Lenehan *et al*., 1996; Parkinson & Evans, 2006). The measures used have not been validated. A limited number of case reports have been published in which the authors attribute the use of anabolic steroids to severe forms of acne including acne conglobata or acne fulminans (Collins & Cotterill, 1995; Gerber *et al*., 2008 (see also (Evans-Brown *et al*., 2008)); Heydenreich, 1989; Merkle *et al*., 1990; Piérard, 1998; Mayerhausen *et al*., 1989; Walker & Parry, 2006).

Male pattern baldness has been shown to be androgen-dependent (Randall, 2004). It is conceivable that in those who are genetically predisposed to this form of scalp hair loss, the use of certain types of steroids could accelerate the progression of hair loss. In cross-sectional questionnaire studies many users report “baldness/hair loss” (presumably scalp hair) (Korkia & Stimson, 1993; Lenehan *et al*., 1996; Grace *et al*., 2001). Conversely, many steroid users report increased growth of body hair when using steroids (Korkia & Stimson, 1993; Lenehan *et al*., 1996). From the limited data available growth of facial hair maybe particularly pronounced in female users (Korkia *et al*., 1996; Strauss *et al*., 1985). Overall, the measures used have not been validated.

Psychological & Behavioral

Aggression and violence

There has been a great deal of interest in the use of anabolic steroids and effects on aggression and violence. It is common for users to self-report increased ‘aggression’ when using anabolic steroids which they suggest they use instrumentally in training (Korkia & Stimson, 1993; Lenehan *et al*., 1996; Monaghan, 2001). The measures used have not been validated. However, there are “conflicts” and contradictions both across the population of users

and within users (Monaghan, 2001). In naturalistic studies there has been a failure to examine potential confounding factors including drug expectancy effects and social factors (such as lifestyle and occupation) (Mazur, 2005). Data from a placebo-controlled randomised trial that used 600 mg/week of testosterone enantate over 10 weeks in healthy young men found no significant changes between control and treatment in self- and observer-rated ('significant other') aggression and anger (Bhasin *et al*., 1996). Conversely, Pope *et al*., (2000) who examined the effect of increasing doses of testosterone cipionate also in a placebo-controlled trial, this time for 6 weeks up to a maximum of 6 weeks found that there appeared to be a few 'responders' in the treatment group, noting that 'drug response was highly variable'. While there was a significant increase in mania scores and aggression scores this effect was not uniform. They conclude "testosterone administration, 600 mg/wk increased ratings of manic symptoms in normal men. This effect, however, was not uniform across individuals; most showed little psychological change, whereas a few developed prominent effects. The mechanism of these variable reactions remains unclear." (Pope *et al*., 2000) (see also Mazur, 2005). Overall, differences in the study design, methods, participants and drug regimens could account for these findings.
A systematic review of this subject concluded that there are currently insufficient data to decide on a causal link between anabolic steroid use and aggressive and violent behaviour.

Depression
Data from cross-sectional studies suggests that some users self-report depression upon ceasing a cycle of steroid use, for example Lenehan *et al*., 1996 found that approximately 20% (n=386) reported this finding. However, there are limited data on this topic using validated scales for depression. Given that steroid use can suppress endogenous testosterone production, it is plausible that when stopping use of these drugs the resultant hypogonadism could cause disturbances to mood, including depression, similar to that seen in clinical populations with hypogonadism (Christiansen, 2004). However, this remains to be systematically examined in steroid users.

Dependence
It is unclear whether anabolic steroids have the potential to cause physical dependence. However, it has been suggested that they can induce psychological dependence in some individuals, although detailed data is limited. For some individuals it is possible that the benefits of steroid use (that include increased training capacity, increased strength, 'enhanced appearance', and feelings of well being) act as a strong reinforcer to continue/recommence use. It is has been suggested that this can be a particularly strong force during an "off" cycle or when ceasing use because of the low levels of endogenous testosterone (anabolic steroid-induced hypogonadism) although this remains to be examined and, currently, there are limited data on this area. Data from cross-sectional studies have found that some users self-report wanting more anabolic steroids when use is stopped (for example Lenehan *et al*., (1996) found 16.9% of users reporting this feeling). Using either semi/structured clinical interviews or self-completed questionnaires typically based on DSM-III-R/DSM IV symptoms, a number of

studies have examined this issue in users. Here three or more symptoms (consistent with a diagnosis of dependence) were reported by 14.3% (n=11/77) (Malone *et al*., 1995), 23% (n=23/100) (Copeland *et al*., 2000), 25% (n=22/88) Pope & Katz (1994), 26% (n=13/50) (Midgley *et al*., 1999), 32% (n=20/62)(Kanayama *et al*., 2009), 33% (n=68/206) (Perry *et al*., 2005), 57% (n=28/49) (Brower *et al*., 1991), 57% (n=12/21) (Gridley & Hanrahan, 1994). Further work is required to validate and determine both the utility and significance of these findings. Overall, differences in the study design, methods and participants could account for these different findings. It is also unclear how representative these groups are of the broader group.

Other Psychological & Behavioural effects

The effects of the use of anabolic steroids on mental health are for the most part drawn from self-reported effects in cross-sectional studies. The measures used often have not been validated. There have also been a limited number of case reports. Reported effects include anxiety, 'mood swings', and insomnia. There have also been a few case reports of suicide; however it is difficult to determine causality in these cases. Data from a retrospective study of mortality in steroid users found that there was no significant difference between the rate of suicide between steroid users and a control group of non-steroid users (Petersson, 2006). However, overall there is limited data on psychological and behavioural effects.

Specific concerns for young people

Adolescence is a complex time of physical, emotional and psychological development which is mediated, in part, by the endogenous equivalents of commonly used performance-enhancing drugs such as testosterone, growth hormone and insulin-like growth factor-1. The use of supraphysiological doses of these drugs during this time in development could, potentially, disrupt the normal pattern of growth and behavioural maturation. This is likely dependent on the specific drugs used, doses taken and duration of use, along with an individual's stage of development. Indeed, early clinical use of anabolic steroids in young people did lead to virilization (see below for effects on females). Further, it has been suggested that use of anabolic steroids in young people whose growth plates in the long bones have not fused could lead to stunted growth. While we are not aware of any such data in relation to illicit steroid use, testosterone esters have been used clinically in adolescent males in an attempt to reduce final height of those with constitutionally tall stature (Drop *et al*., 1998). Here the authors report that the doses that have been used "correspond to roughly 4 times the normal T production rate of adult men or to about 8–10 times that of early adolescence", although the authors note that prospective controlled studies are required to determine if this treatment is effective in reducing final height.

Specific concerns for females

Given the low endogenous levels of testosterone in females, any increase through endogenous sources (such as in disease states) and, by analogy, exogenous sources (i.e. anabolic steroids) can have marked physical effects, and can lead to virilisation which includes: hirsutism, deepening of the voice, amenorrhoea/anovulation, clitoral enlargement, atrophy of breast tissue, and

changes in libido. The impact of these effects can be pronounced, and, in some cases, permanent. There are limited data in relation to these effects in female steroid users, due to the relatively small numbers of users and compounded by the clandestine nature of use amongst this sub population. Most data are derived from self-reports (Korkia *et al*., 1996; Strauss *et al*., 1985).

Injecting
Background

Data from the United Kingdom suggests that the majority of users inject anabolic steroid (ranging from 59.6% (Bolding *et al*., 1999) to 89% (Grace *et al*., 2001), with most studies reporting that ≥70% inject (Burton, 1996; Grace *et al*., 2001; Korkia & Stimson, 1993; Lenehan *et al*., 1996; Pates & Barry, 1996). These figures include a majority that both inject and take oral drug products and a minority that exclusively use injectable products. Limited data are available on the routes of administration for the small number of female users, however it appears that many of these also inject (Korkia & Stimson, 1993; Korkia *et al*., 1996).

Individuals who inject are potentially at risk of a number of sequelae that include: 1. damage to the injection site as a result of poor injecting technique; 2. bacterial and fungal infections as a result of poor injecting technique, contaminated drug products, and sharing vials and/or reusing injecting equipment; and, 3. blood-borne viruses (BBV) such as HIV, hepatitis B and hepatitis C as a result of sharing used injecting equipment (direct sharing) or reusing injecting equipment and, subsequently, sharing vials with others (indirect sharing).

Limited data are available on injecting practices in users within the UK (Baker *et al*., 2006; Burton, 1996; Evans, 1997; Grace *et al*., 2001; Korkia & Stimson, 1993; Lenehan *et al*., 1996; Midgley *et al*., 2000; Pates & Barry; 1996) (Table 1). Both studies conducted by Bolding *et al*., (1999; 2002) with gay/bisexual users in London gyms found no direct sharing (Bolding *et al*., 1999; Bolding *et al*., 2002). Other studies have found relatively low-levels of lifetime direct sharing: 0.3% (Lenehan *et al*., 1996), 2.1% (Midgley *et al*, 2000), 5.7% (Korkia & Stimson, 1993), 6% (Crampin *et al*., 1998); while Burton (1996) reported 16% and Grace *et al*., (2001) 20% “at times when they [syringes] were not readily available”. However, these latter papers do not provide data on the frequency of sharing (i.e. whether it was lifetime, last month, etc); it is unclear what is responsible for the large variation in reports of sharing between studies. A subset of these studies also examined indirect sharing, particularly through the use of multi-dose vials. This behaviour could be a source of infection, notably BBVs, if this co-occurs with the reuse of injecting equipment. Further, it is possible that the sharing of multi-dose vials (particularly in non-salubrious environments) where basic hygiene measures are not followed (and/or storage and handling measures for drug products are not adequate) could increase the risk of bacterial and fungal contamination. Although we are not aware of any research in relation to this context, data from clinical settings have suggested that contamination has taken place

leading to iatrogenic infections (Kirschke *et al*., 2003; Thompson *et al*., 2009; Vonberg & Gastmeier, 2007).

	Korkia & Stimson (1993)	**Lenehan *et al*., (1996)**	**Pates & Barry (1996)**	**Burton (1996)**	**Crampin *et al*., (1998)**	**Bolding *et al*., (1999) ¶**	**Midgely *et al*., (2000)**	**Grace *et al*., (2001)**	**Bolding *et al*., (2002) ¶**
"Ever" shared	5.7% (5/88)	0.3% (1/386)	1.74% (3/176) †	16%	6% (8/134)	0%	2.1% (1/47)	20%	0
Shared last month	N/A	N/A	N/A	N/A	≤1% (1/134)	N/A	N/A	N/A	N/A
"Ever" shared multi-dose vial (a)	N/A*	N/A	N/A	59%	N/A	9.9% (8/81)	23.4% (/47)	N/A	2.4% (2/85)
"Ever" reuse injecting equipment (b)	N/A	N/A	N/A	37%	N/A	7.4% (6/81)	4.2% (2/47)	N/A	8.2% (7/85)
Reporting both behaviours (a + b)	N/A	N/A	N/A	N/A	N/A	3.7% (3/81)	4.2% (2/47)	N/A	1.2% (1/85)

† "admitted to sharing, borrowing or passing on needles and syringes". *There were anecdotal reports about the sharing of injecting equipment and of multi-dose vials. ¶ Study examined the use of anabolic steroids by gay/bisexual users.

Table. Data on direct and indirect sharing in anabolic steroids users from UK studies.

Burton (1996) found that 59% of steroid injectors reported sharing multi-dose vials with other users and 37% having reused their 'needles', although no data are available on the co-occurrence of these two behaviours which would be required in order to pose a risk of transmission of infections. Data from three studies (see Table 1) have found these two behaviours in 3.7% (3/81) (Bolding *et al*., 1999), 4.2% (2/47) (Midgely *et al*., 2000), and 1.2% (1/85) (Bolding *et al*., 2002) of users. Again, no data on co-occurrence are reported.

Damage to the injection site

There have been several case reports of peripheral neuropathy that the authors attribute to injecting anabolic steroids (Dickerman *et al*., 1997; Evans,

1997; Mondellie *et al*., 1998; Perry, 1994) or muscular hypertrophy leading to nerve compression (Dickerman *et al*., 2002). While the incidence of these sequelae are unknown, data from Larance *et al*., (2008) found that 10% (n=31) of users self-reported hitting a nerve when injecting (however, it is unclear how users determined this and how representative this group was). There has also been a small number of case reports of 'pseudotumours' (Khankhanian *et al*., 1992; Kienbacher *et al*., 2007; Weinreb *et al*., 2010). The aetiology of these could be due physical trauma from the injection process, a tissue reaction to the drug product or contaminant therein. Akhavani *et al*., (2006) reported a case of compartment syndrome in an anabolic steroid user which they believe was as a result of intramuscular injection of an anabolic steroid. Again, the incidence of such sequelae is unknown.

Bacterial and fungal infections

There have been a small number of case reports of bacterial and fungal infections that the authors attribute to injecting anabolic steroids. Typically these have presented as localised infection such as abscesses (Al-Ismail *et al*., 2002; Bergman, 1993; Cooper *et al*., 1993; Dunn *et al*., 2002; Evans, 1997; Gautschi & Zellweger, 2006; Herr *et al*., 2002; Kienbacher *et al*., 2007; Krauss *et al*., 1995; Larsen & Halvorsen, 2000; Maropis & Yesalis, 1994; Marquis & Maffulli, 2006; Plaus & Hermann, 1991; Rastad *et al*., 1985; Rich *et al*., 1999). The aetiology of these infections could be due to poor injecting technique and/or contamination of injectable dosage forms (the latter of which could occur as a result of poor injecting technique, microbial contamination during manufacture/distribution (Evans-Brown *et al*., 2009) or sharing multi-dose vials). The incidence of these types of sequelae are unknown. Self-reported lifetime data from cross-sectional studies from Australia and the United States have found that 13% (n=100) (Peters *et al*., 1997) and 13% (n=60) (Larance *et al*., 2005) of users reported "buttock abscess" (Australia, face-to-face structured interviews); while Cohen *et al*., found that 7% (n=1,955 males) reported "infections resulting from injection" (US, Internet-based study). The lifetime report of "sore/swollen injection sites" was 57% (n=100) (Peters *et al*., 1997) and 45% (n=60) (Larance *et al*., (2005). "Pain at injection sites" was reported by 36.4% (39/111) by Bolding *et al*., (2002), although it is not clear if this was as a result of infection or trauma caused by the injecting process. Larance *et al*., (2008) found that 13% (n=31) of users reported an "infection that required treatment with antibiotics"; while 3% (n=31) reported "injection-related problem requiring hospitalisation". The interpretation of these data is complicated by the use of different methodologies between studies and the lack of concurrent validity. Further it is unclear how representative these groups are of the broader user group. Aside from the three case reports list above (Evans, 1997; Dunn *et al*., 2002; Marquis & Maffulli, 2006), we are not aware of any further data from the United Kingdom.

Blood-borne viruses

There are limited data in relation to the prevalence and transmission of BBVs in anabolic steroid users within the UK. There have been a small number of case reports from France and the United States that the authors attribute to the direct sharing of injecting equipment to HIV (Scott & Scott, 1989; Sklarek *et al*., 1984; Henrion *et al*., 1992), hepatitis B (Slarek *et al*., 1984) and

hepatitis C (Coton *et al*., 2000; Rich *et al*., 1998) infection. However, it is difficult to draw any firm conclusions from these data given aetiological confounding factors These cases do, however, demonstrate that direct sharing within this user group has taken place.

To our knowledge, the work of Crampin *et al*., (1998) is the only published study that has examined HIV and hepatitis B exposure in anabolic steroid users attending needle and syringe programmes (NSP) in the United Kingdom. They analysed data from 1991–1996 derived from the national Unlinked Anonymous HIV Prevalence Monitoring Survey of injecting drug users. Here they found that 2% (3/149) of users had evidence of previous or current hepatitis B infection, while none had antibodies to HIV. The study did not examine hepatitis C exposure. Since this time there has been significant epidemiological shifts in HIV and hepatitis C infection in the UK (Health Protection Agency Centre for Infections, 2006; Health Protection Agency Centre for Infections, 2008)). Data from Bolding *et al*., (2002) who studied anabolic steroid use in gay/bisexual users in London found that 36.7% (40/109) of those that had used steroids in the past year self-reported being HIV-positive (no participants reported direct sharing and the only individual to report both sharing multi-dose vials and reuse of injecting equipment self-reported as being HIV-negative. It is unknown if these two behaviours co-occurred (Bolding *et al*., 2002)). The number of HIV-positive individuals within these samples could be a reflection of both clinician-prescribed (Johns *et al*., 2005) and self-directed use (Mooney & Vergel, 2004) of anabolic steroids as a prophylactic/treatment for HIV/AIDS-related wasting.

While the risk of BBV transmission in anabolic steroid users appears to be low when compared to other groups, such as those injecting opiates and stimulants (Health Protection Agency, 2007), the practices and risks remain poorly characterised. Importantly, any such work that is undertaken must include those individuals who are not in contact with NSPs, as despite the extensive peer distribution network that appears to exists (Gilliver, 2007; McVeigh *et al*., 2007), their injecting practices may differ significantly from their peers who do attend NSPs. This is particularly relevant for younger users, where it has been reported that they will not attend NSPs for fear of being labelled as an injecting drug user (Personal communication to Michael Evans-Brown, 2008).

Annex F. Case Studies of Specific Services developed for Anabolic Steroid Users

1 Drugs in Sport Clinic and Users' Support (DISCUS)

The clinic started in 1994 with both specialist medical and nursing input and now has more than 1,000 patients registered. Alongside the NSP (where some users are collecting injecting equipment for up to 250 users), DISCUS provides testing for BBV and immunisation for hepatitis A and B, regular blood investigations, specialist dietary services (inc. body fat analysis), and referral to other services where necessary.

2 Smart Muscle (not currently operating)

Smart Muscle builds upon the previous work of SUSSED which included specific interventions focussed on anabolic steroid use within the gay community. Part of the social care organisation Turning Point, Smart Muscle is a central London service that is free and confidential. It provides information on diet, training, cycles, stacks, post-cycle therapy, side effects and help to identify counterfeit drugs. Needle and syringe exchange (using pick-and-mix) is available to complete their course and advice is provided to ensure that their injection technique is correct (if they choose to inject). The service has a partnership with the local GUM service who offers liver function testing, vaccinations for hepatitis A and B, along with full sexual health screens. The service does refer clients to specialist services as required. In the last 18 months Smart Muscle has provided services to 299 users, from ages 18–70, with the majority of users aged 22–50. 70% of clients have identified themselves as gay or bisexual and 12 clients reported themselves as HIV positive.

3 Surrey Harm Reduction Outreach Service

Established in 1992, this project provides information, advice and health checks via a network of NSP and drop-in centre. However, the key innovative element of the approach is the use of specialist outreach workers to maintain close links with the anabolic steroid-using communities.

4 Wirral Harm Reduction Service

Harm reduction services for anabolic steroid users in the Wirral have been available since the 1990s. The intervention is nurse-led incorporating NSP, harm reduction, general health checks, sexual health screening and specialist referrals as required.