Doc. 560-32 Defendants' Summary Judgment Exhibit 182 (Redacted)

WPATH Standards of Care- 8th

Chapter X: Hormone Therapy for Trans and Gender Diverse Adolescents and Adults

INTRODUCTION

Transgender and gender diverse (TGD) persons may request gender affirming hormone therapy (GAHT) to better align their bodies with their gender identity. Gender affirming hormone therapy has been accepted as medically necessary since the first WPATH SOC published in 1979 and subsequent updates of the SOC including SOC version 7 (Coleman et al., 2012). WPATH endorsed the Endocrine Society's guidelines on gender affirming hormone therapy for TGD persons in 2009 and 2017(Hembree et al., 2009; Hembree et al., 2017). The European Society for Sexual Medicine has also published a position statement on hormone management in adolescent and adult TGD people (T'Sjoen et al 2020). Under medical supervision, GAHT in adults is safe (Weinand JD et al., 2015). However, there are some potential long-term risks that require careful monitoring and screening to reduce adverse events (Hembree et al., 2017, Tangpricha et al 2019).

The approach to GAHT differs depending on the developmental stage of the individual at initiation of hormone therapy and their treatment goals. Hormone therapy is not recommended for children who have not begun endogenous puberty. In youth who have reached the early stages of puberty, the focus is usually to delay further pubertal progression with gonadotropin releasing hormone agonists (GnRHa) until an

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appropriate time to introduce GAHT. Adults may initiate on GAHT when they are able to provide informed consent, clearly articulate gender identity and goals for treatment, and have any medical or mental health concerns addressed. Medical providers should discuss fertility goals and fertility preservation options prior to initiating GAHT (see chapter on reproductive health).

Feminizing GAHT typically consists of estrogen and an androgen lowering medication. Although there are anecdotal reports of progesterone use for breast development and mood, there is insufficient evidence that potential progesterone benefits would outweigh potential risks (Iwamoto et al., 2019). Masculinizing GAHT typically consists of testosterone. Both WPATH and the Endocrine Society recommend monitoring levels of sex hormones. While GAHT is customized to the needs of the TGD person, it is typical for hormone levels to be at least sufficient for good bone health and not supraphysiologic (Hembree et al, 2017, Rosen et al 2019).

In most cases, GAHT is maintained throughout life. It is not known if doses of GAHT should be reduced in older TGD people. Discontinuation of hormone therapy may result in bone loss in both transfeminine and transmasculine individuals (Wiepjes et al 2020). Routine primary care should also be performed (see chapter on primary care). There are reports of increased cardiovascular disease and venous thromboembolism in TGD on estrogen treatment in epidemiological studies, more notable in older women or with different preparations of GAHT (Maraka et al, 2017, Irwig MS, 2018). TGD individuals on testosterone may also have increased adverse cardiovascular events due to an increase in blood pressure, decrease in HDL-cholesterol and excess weight (Irwig MS, 2018). Clinicians should discuss lifestyle

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and pharmacologic therapy in those at highest risk of cardiovascular disease (see chapter on primary care). Polycythemia may be unmasked in TGD on testosterone treatment (Antun et al, 2020). Monitoring of conditions that can be exacerbated by GAHT is important throughout life (Hembree et al, 2017)

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Summary of Recommendations

Youth

Timing of the start of puberty suppression

1. We recommend that clinicians should begin pubertal hormone suppression in eligible trans and gender diverse adolescents after they first exhibit physical changes of puberty (Tanner stage 2) (87.49%) +++

Methods of puberty suppression

2. We recommend that clinicians should use GnRH agonists, for trans and gender diverse patients where puberty blocking is indicated, to suppress endogenous sex hormones. (78.78%) +++

3. We suggest that clinicians should prescribe progesterone (oral or injectable depot) in transgender youth for pubertal suspension when GnRH agonists are not available or cost prohibitive. (88 %) ++

4. We suggest that clinicians prescribe GnRH agonists for suppression of sex steroids without concomitant sex steroid hormone replacement in adolescents seeking such intervention who are well into or finished with pubertal development (past Tanner stage 3) but are unsure about or do not desire to begin sex steroid hormone therapy. (82%) ++

5. We suggest that clinicians should prescribe sex hormone treatment regimens as part of gender affirming treatment in eligible adolescents who are at least Tanner 2, preferably with parental/guardian consent, and that treatment decisions should be made among the adolescent, parents/guardians, and treatment team. (79.54%) ++

Timing and method of starting gender affirming hormones in youth

6. We recommend that clinicians should measure hormone levels during gender affirming treatment to ensure that endogenous sex steroids are lowered and administered sex steroids are maintained as appropriate to the treatment goals of trans and gender diverse patients according to Tanner stage. (91.92%) +++

7. We recommend that clinicians should prescribe progestogens or a GnRH agonists in transgender adolescents with a uterus to reduce dysphoria caused by their menstrual cycle when androgen therapy is not yet indicated. (91%) +++

8. We suggest that clinicians involve professionals who are experts in transgender health from multiple disciplines in the management of the care of trans and gender diverse adolescents (76.46%) ++

Youth and Adults

Initiation of Hormone Therapy and Fertility Considerations

9. We recommend that clinicians should organize regular clinical evaluation for physical changes and potential adverse effects in response to sex steroid hormones and laboratory monitoring of sex steroid hormone every 3 months during the first year of hormone therapy or with dose changes until stable adult dosing is reached followed by clinical and laboratory testing once or twice a year once an adult maintenance dose is reached. (88.88%) +++

10. We recommend that clinicians should inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression and prior to treating with hormonal therapy (97.08%) ++

11. We recommend that clinicians should evaluate and address medical conditions that can be exacerbated by lowered endogenous sex hormone concentrations and treatment with exogenous sex hormones before beginning treatment in trans and gender diverse people. (86.14%) ++

12. We recommend that clinicians should educate trans and gender diverse patients undergoing gender affirming treatment about the onset and time course of physical changes induced by sex hormone treatment. (96.11%) ++

Gender Affirming Hormone Regimens

13. We recommend that clinicians should not prescribe ethinyl estradiol in transgender youth and adults as part of a gender affirming hormone treatment (91%) +++

14. We suggest that clinicians should prescribe transdermal estrogen in transgender youth and adults who have been recommended gender affirming estrogen treatment when they are at higher risk of VTE based on age >45 years or have previous history of VTE. (89%) ++

15. We suggest that clinicians should not prescribe conjugated estrogens in transgender youth and adults when estradiol is available as part of gender affirming hormone treatment. (94%) ++

16. We recommend that clinicians prescribe testosterone lowering medications (either cyproterone acetate, spironolactone or GnRH agonist) for transgender youth and adults with testes taking estrogen as part of a hormone treatment plan if their individual goal is to approximate circulating sex hormone concentrations of cisgender women. (88%) +++

17. We recommend that clinicians should monitor hematocrit (or hemoglobin) in transgender youth and adults treated with testosterone. (96%) +++

Preparation for Gender Affirming Surgeries

18. We suggest that clinicians should collaborate with surgeons regarding hormone use before and after gender affirming surgery. (82.96%) ++

19. We suggest that clinicians should counsel patients on the various options for gender-affirming surgery on trans and gender diverse patients, unless surgery is not desired or medically contraindicated. (78.65%) ++

20. We recommend that clinicians should initiate and continue gender-affirming hormone therapy in transgender youth and adults who wish this treatment due to demonstrated improvement of psychosocial functioning and quality of life. (88%) +++

21. We recommend that, unless contraindicated, clinicians should maintain existing hormone therapy if TGGD individual's mental health deteriorates, and assess the reason for the deterioration. (89%) ++

Footnote: Percentages refer to the passing rate by the Delphi process. Statements supported by systematic literature review are rated as follows: ++++ strong certainty of evidence, +++ moderate certainty of evidence, ++ low certainty of evidence, + very low certainty of evidence

Gender Affirmation Hormone Therapy in Youth

The following sections will discuss hormone therapy in TGD youth. Depending on the developmental stage of the youth, this generally consists of two phases: pubertal suppression followed by the addition of GAHT. During the first phase, pubertal development is halted to allow youth to explore their gender identity and prepare for the next phase which may include GAHT. This section will discuss the recommendations regarding the use of gonadotropin releasing hormone agonists (GnRHa) as well as alternate approaches to pubertal suppression. This will be followed by recommendations on gender affirming hormone treatment. Sections that are applicable to youth and adults will follow in the next section.

Approaches to pubertal suppression in eligible adolescents

Timing of the start of puberty suppression

1. We recommend that clinicians should begin pubertal hormone suppression in eligible trans and gender diverse adolescents after they first exhibit physical changes of puberty (Tanner stage 2). (87.49%) +++

In general, the goal of the use GnRHa in transgender adolescents is to prevent the further unwanted development of the endogenous secondary sex characteristics corresponding to the sex assigned at birth. Since this treatment is still fully reversible, it is regarded as an extended time for adolescents to explore their gender identity through an early social transition (Ashley, 2019). Treatment with GnRHa also has some therapeutic effects since it often results in a vast reduction of the distress stemming

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from unwanted physical changes from the initiation of endogenous puberty(Rosenthal, 2014, de Vries, et al., 2011).

In addition, the suppression of the development of secondary sex characteristics is most effective when sex hormone treatment is initiated in early to mid-puberty as compared to when sex hormone treatment is initiated after puberty is completed (Bangalore-Krisha K., et al). Correspondingly, adolescents who have already completed endogenous puberty and are considering starting GAHT can use GnRHa to inhibit unwanted physical functions, such as menses or erections to bridge the period until the adolescent, guardian(s) (if the adolescent is not able to consent independently) and treatment team can make the decision (Bangalore-Krishna, K., et al, 2019)

The onset of puberty occurs through reactivation of the hypothalamic-pituitary-gonadal axis. Clinical assessment of the stages of puberty is based on physical features that reflect that reactivation. In individuals with functioning ovaries, Tanner stage 2 is characterized by the budding of the mammary gland. The development of the mammary gland occurs from the exposure to estrogen produced by the ovaries. In individuals with functioning testes, Tanner stage 2 is characterized by the increase of testicular volume. The growth of the testes is mediated through the gonadotropins (luteinizing hormone (LH) and follicle stimulating hormone (FSH). In the later stages, the testes produce enough testosterone levels to induce virilization of the body (Palmert, M., et al, 2021).

Methods of puberty suppression

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2. We recommend that clinicians should use GnRH agonists, for trans and gender diverse patients where puberty blocking is indicated, to suppress endogenous sex hormones. (78.78%) +++

3. We suggest that clinicians should prescribe progesterone (oral or injectable depot) in transgender youth for pubertal suspension when GnRH agonists are not available or cost prohibitive. (88%) ++

4. We suggest that clinicians prescribe GnRH agonists for suppression of sex steroids without concomitant sex steroid hormone replacement in adolescents seeking such intervention who are well into or finished with pubertal development (past Tanner stage 3) but are unsure about or do not desire to begin sex steroid hormone therapy. (82%) ++

GnRHa reduce gonadotrophin and sex steroid concentrations in transgender adolescents and thus halting the further development of secondary sex characteristics (Bangalore-Krishna, K., et al., 2019, Schagen, Cohen-Kettenis, Delemarre-van de Waal, & Hannema, 2016). Their use is generally safe with the only short-term adverse event reported the development of arterial hypertension (Delemarre-van de Waal & Cohen-Kettenis, 2006; D. Klink, Bokenkamp, Dekker, & Rotteveel, 2015). GnRHa prevents the pituitary gland from secreting LH and FSH (Gava G et al, 2020). When the gonadotropins decrease, the gonad is no longer stimulated to produce sex hormones (estrogens or androgens) and the sex hormone levels in the blood decrease to prepubertal levels. GnRHa treatment will lead to partial regression of the initial stages of the already developed secondary sex characteristics (Bangalore, K et al, 2019). TGD adolescents with functioning ovaries will experience diminished growth of the breast tissue, and if treatment is started at Tanner Stage 2, the breast tissue may disappear

completely. Menarche can be prevented or discontinued following GnRHa in adolescents with a uterus. In TGD adolescents with functioning testes, testicular volume will regress to a lower volume.

When GnRHa treatment is started in adolescents at the later phases of pubertal development, some physical changes of pubertal development, such as a late stage of breast development in TGD adolescents with functioning ovaries and lowering of the voice and growth of facial hair in TGD adolescents with functioning testes, will not regress completely, although any further progression will be stopped(Bangalore-Krishna, et al., 2019, Delemarre-van de Waal & Cohen-Kettenis, 2006). GnRHa have been used since 1981 in the treatment of central precocious puberty(Comite et al., 1981; Laron, Zeev, Kauli, Comaru-Schally, & Schally, 1981) and their benefits are well established. The use of GnRHa in central precocious puberty is regarded as both safe and effective, with no known long-term adverse effects (Carel et al., 2009, Kim et a., 2015, Liu et al, 2016, Bertelloni et al, 2008). However, the use of GnRHa in transgender adolescents are considered off-label because they were not initially developed for this purpose. However, data from adolescents prescribed GnRHa in a similar dose and fashion demonstrate effectiveness in delaying the onset of puberty although the long-term effects of bone mass are not well established. Although long term data are more limited in TGD adolescents compared to adolescents with precocious puberty, data collection are ongoing specifically in this population(Klaver et al., 2020; Lee et al., 2020; Millington et al., 2020; Olson-Kennedy et al., 2019) .

We recognize that in eligible adolescents, GnRHa may not be available, because it is not covered by health coverage plans or may be cost-prohibitive. Therefore, other

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approaches, including oral or injectable progesterone formulations should be considered in these cases. In addition, in adolescents older than 14, we do not currently have the data to inform whether GnRH agonists, as mono-therapy, can be used (and for what duration) without posing significant risk to skeletal health. This is because the skeleton will not have any exposure to adequate levels of sex steroid hormones.

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life (Finkelstein JS et al, 1996, Bertelloni S et al, 1998). Move this citation earlier

Prolonged hypogonadal state in adolescence, whether due to medical conditions, such as hypergonadotropic hypogonadism or iatrogenic due to GnRHa monotherapy or physiological conditions, such as conditional delay of growth and development may be associated with risk towards bone health later in life (Finkelstein JS et al, 1996, Bertelloni S et al, 1998). However, bone mass accrual is a multifactorial process of the interplay of endocrine, genetic and lifestyle factors (Anai T, et al 2001). When deciding on the duration of GnRHa monotherapy, all contributing factors should be taken into account. From an endocrine perspective, factors such as pre-treatment level of bone mass, bone age, and pubertal stage should be considered. From a psychosocial perspective, factors such as growth and developmental stage relative to cohort and the adolescent's individual treatment goals, should be considered. In addition, the clinical course of the treatment, i.e. the development of bone mass under GnRHa treatment and the adolescent's response to treatment, can help to determine the length of GnRHa monotherapy.

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Timing and method of start gender affirming hormones in youth

5. We suggest that clinicians should prescribe sex hormone treatment regimens as part of gender affirming treatment in eligible adolescents who are at least Tanner 2, preferably with parental/guardian consent, and that treatment decisions

should be made among the adolescent, parents/guardians, and treatment team. (79.54%) ++

6. We recommend that clinicians should measure hormone levels during gender affirming treatment to ensure that endogenous sex steroids are lowered and administered sex steroids are maintained as appropriate to the treatment goals of trans and gender diverse patients according to Tanner stage. (91.92%) +++

Sex steroid hormone therapy generally has two treatment regimens, depending on the timing of the GnRHa treatment. When GnRHa treatment is started in the early stages of endogenous pubertal development, a puberty corresponding with gender identity is induced with doses of sex steroid hormones similar to those used in peri-pubertal hypogonadal adolescents. In this context, adult doses of sex steroid hormones are typically reached over approximately a 2-year period. (Chantrapanichkul et al, 2021) When GnRHa treatment is started in late-pubertal or post pubertal transgender adolescents, sex steroid hormones can be given at a higher starting dose and more rapidly increased until a maintenance dose is achieved, resembling treatment protocols used in transgender adults (Hembree et al 2017). An additional advantage of GnRHa treatment is that sex steroid hormones do not have to be administered in supraphysiological dosages, which would otherwise be needed to suppress endogenous sex steroid production(Safer & Tangpricha, 2019). For TGD individuals with functioning testes, GnRHa treatment (or another testosterone blocking medication) should be continued until such time as the transgender adolescent/young adult ultimately undergoes gonadectomy, if this surgical procedure is chosen as part of their gender-affirming care. For TGD individuals with functioning ovaries, initially suppressed with GnRHa, once adult levels of testosterone are reached, testosterone alone, at

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physiological doses, is typically sufficient to inhibit ovarian estrogen secretion, and GnRHa can be discontinued, as discussed below (Hembree et al 2017). For TGD adolescents with functioning ovaries and are new to care, transition can be accomplished with physiological doses of testosterone alone, without need for concomitant GnRHa administration (Hembree et al 2017)

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Gender-affirming sex steroid hormone therapy induces the development of secondary sex characteristics of the gender identity. Also, the rate of bone mineralization, which decreases during treatment with GnRHa, rapidly recovers(Klink et al., 2014). During GnRHa treatment in early pubertal transgender TGD adolescents, the bone epiphyseal plates are still unfused (Kvist et al, 2020, Schagen, S., et al 2020). Following the initiation of sex steroid hormone treatment, a growth spurt can occur, and bone maturation will continue (Vlot et al, 2017). In post-pubertal transgender adolescents, sex steroid hormone treatment will not affect height since the epiphyseal plates have fused and bone maturation is complete (Vlot et al, 2017).

In TGD adolescents with functioning testes, the use of 17-beta estradiol for pubertal induction is preferred over synthetic estrogens, such as ethinyl estradiol which have a more thrombogenic profile (see recommendations for sex steroid hormones in transgender adults) (Asscheman et al, 2015). It is still necessary to continue the GnRHa to suppress endogenous testosterone production or transition to another medication that suppresses endogenous testosterone production (see recommendations for sex hormones in transgender adults) (Rosenthal et al, 2016). Estrogen treatment results in physical changes such as breast development and a female fat distribution among other physical changes (Table 1).

For TGD adolescents seeking masculinizing treatment, androgens are available as injectable preparations, transdermal formulations and subcutaneous pellets. For pubertal induction, the use of testosterone-ester injection is recommended initially due to cost, availability and experience (Shumer et al, 2016). It is advised to continue GnRHa at least until a maintenance level of testosterone is reached. In response to androgen treatment, virilization of the body occurs: lowering of the voice, more muscular development, particularly in the upper body, facial and body hair growth and clitoral enlargement (Rosenthal et al, 2016)(Table 1).

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7. We suggest that clinicians should prescribe progestogens or GnRH agonists in transgender adolescents with a uterus to reduce dysphoria caused by their menstrual cycle when androgen therapy is not yet indicated. (91%) +++

Menstrual suppression is a treatment option commonly requested by TGD individuals who experience distress related to menses or anticipation of menarche. Menstrual suppression can be initiated as a solo option, before initiating testosterone, or alongside testosterone therapy in order to achieve amenorrhea(Carswell & Roberts, 2017). Some youth who are not ready for or not yet at an appropriate pubertal/developmental stage to begin testosterone therapy are interested in induction of amenorrhea(Olson-Kennedy, Rosenthal, Hastings, & Wesp, 2018). Adolescents who experience an exacerbation of dysphoria related to the onset of puberty may elect to be treated with GnRHa for pubertal suppression.

Progestogens may be effective for adolescents whose goal is solely menstrual suppression. Continuous administration of progestin-only oral pills (including the

contraceptive and non-contraceptive options), medroxyprogesterone injections, or levonorgestrel intrauterine device can be used for induction of amenorrhea(Pradhan & Gomez-Lobo, 2019). As most TGD individuals with functioning ovaries who start testosterone therapy may have 1-3 menstrual cycles before amenorrhea is achieved, some may opt to start menstrual suppression treatment alongside testosterone therapy. Once amenorrhea is achieved, some TGD individuals with functioning ovaries may also choose to continue progestin treatment for birth control if relevant to their sexual practices.

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TGS individuals with functioning ovaries and uterus should be counseled on the potential for breakthrough menstrual bleeding in the first few months after initiating menstrual suppression. With GnRHa therapy, breakthrough bleeding may occur 2-3 weeks after initiation of the medication. For individuals seeking contraception or for those who continue to experience menstrual bleeding on progestin therapy, an estrogen combination with progestin may be considered for maintenance of amenorrhea(Schwartz, A. et al., 2017).

8. We suggest that clinicians involve professionals who are experts in transgender health from multiple disciplines in the management of the care of trans and gender diverse adolescents (76.46%) ++

As with the care of adolescents, we suggest where possible that an expert multidisciplinary team of medical and MHPs manage this treatment. In adolescents who request sex steroid hormone treatment (given this is a partly irreversible treatment), we suggest initiating treatment using a gradually increasing dose schedule after a multidisciplinary team of medical and MHPs has confirmed the persistence of

GD/gender incongruence and enough mental capacity to give informed consent(Hembree et al., 2017) .

If possible, trans and gender diverse adolescents should have access to experts in pediatric transgender health from multiple disciplines including primary care, fertility, mental health, voice, social work, spiritual support, and surgery(Chen et al., 2016; Eisenberg, McMorris, Rider, Gower, & Coleman, 2020; C. L. Keo-Meier & Ehrensaft, 2018) . Individual providers are encouraged to form collaborative working relationships with providers from other disciplines to facilitate referrals as needed by the individual youth and family(Tishelman et al., 2015). The lack of available experts and resources should not constitute a barrier to care (Rider et al., 2019). Helpful supports for adolescents include access to accurate, culturally informed information related to gender and sexual identities, transition options, the impact of family support, and connections to others with similar experiences and trans adults through online and in person support groups for adolescents as well as family members(Rider et al., 2019)

As trans and gender diverse adolescents have been found to experience mental health disparities, initial mental health screening (e.g., PHQ-2, GAD) should be routine practice with referrals as indicated (Rider et al., 2019) . Providers should keep in mind that being transgender or questioning one's gender does not constitute pathology or a disorder, therefore individuals should not be referred to mental health services on the basis of a transgender identity. Providers making referrals as well as the mental health providers treating these youth should, at a minimum, be familiar with the impacts of trauma, gender dysphoria, and gender minority stressors on mental health symptomatology including disordered eating, suicidal ideation, social anxiety, etc., as

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well as the readiness of inpatient mental health services in your region to provide competent, gender affirming care to trans and gender diverse youth(Barrow & Apostle, 2018; Kuper, Adams, & Mustanski, 2018; Kuper, Mathews, & Lau, 2019; Tishelman & Neumann-Mascis, 2018) . Because parents of these youth commonly experience high levels of anxiety immediately after learning their youth is TGD, and their response to their child predicts long-term health and mental health outcomes of the child, appropriate referrals for mental health support of the parents can be of great utility(Coolhart, Ritenour, & Grodzinski, 2017; Pullen Sansfaçon, Robichaud, & Dumais-Michaud, 2015; Taliaferro, McMorris, Rider, & Eisenberg, 2018) .

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Commented [redacted]: What is conflicting? Please specify. Perhaps you are not aware of the social determinants and minority stressors, i.e., 3rd variables, that mediate and moderate the relationship between trans identity and health and mental health disparities? I did not think that needed to be fleshed out here, but can do so. Let me know. I would strongly prefer not to leave this section to the adolescent chapter, as this is one of my main contributions.

Initiation of Hormone Therapy and Fertility Considerations in Youth and Adults

9. We recommend that clinicians should organize regular clinical evaluation for physical changes and potential adverse effects in response to sex steroid hormones and laboratory monitoring of sex steroid hormone every 3 months during the first year of hormone therapy or with dose changes until a stable adult dosing is reached followed by clinical and laboratory testing once or twice a year once an adult maintenance dose is reached. (88.88%) +++

Sex steroid hormone therapy is associated with a broad array of physical and psychological changes (Irwig, 2017; Tangpricha & den Heijer, 2017) (**Table 1**). After an individual begins sex steroid hormone therapy, the clinician should regularly assess the progress and response of the individual to the treatment. This evaluation should assess any physical changes and the impact of treatment on gender dysphoria (if present) and psychological well-being (**Table 1**). Clinical visits provide important opportunities for a clinician to educate an individual on realistic expectations regarding the typical time

course for physical changes. During the first year of hormone therapy, sex steroid hormone doses are often increased. A major factor to guide the doses of sex steroid hormones is the serum levels of the corresponding sex steroid hormones. In general, the goal is to target the serum levels of the sex steroids to match the reference ranges of the individual's gender identity, although optimal target ranges have not been established (Hembree et al, 2017).

In addition to assessing the positive changes associated with sex steroid hormone therapy, the clinician should regularly assess whether the treatment has caused any adverse effects (**Table 2).** Examples of adverse signs and symptoms include androgenic acne or bothersome sexual dysfunction (Braun et al., 2021, Kerckhof et al, 2019). Gender affirming hormone treatment also has the potential to adversely affect several laboratory tests. For example, spironolactone use in may cause hyperkalemia although it is an uncommon and transient phenomenon (Millington et al, 2019). Testosterone therapy increases the red blood cell count (hematocrit) which may occasionally cause erythrocytosis (Antun et al, 2020) (see recommendation on monitoring transgender individuals on testosterone therapy) (Hembree et al, 2017). Both estrogen and testosterone therapy can cause changes to lipid parameters such as high-density protein lipoprotein (HDL) cholesterol and triglycerides(Maraka et al., 2017) (see recommendations for primary care in transgender individuals).

The frequency of the clinical evaluations should be individualized and guided by the individual's response to treatment. We suggest clinical assessments approximately every three months during the first year of hormone therapy in patients who are stable and do not experience significant adverse effects (**Table 5**). We suggest rather than

recommend the testing every three months in the first year to allow some flexibility on the timing of these tests as there are no strong evidence or published studies on the interval of testing. More frequent laboratory testing and/or clinical visits are often needed if an individual does experience an adverse effect. Given the potential harms resulting from sex hormone levels that could exceed expected ranges in humans, we have a strong recommendation that regular testing should be performed as standard practice when starting transgender and gender diverse individuals on GAHT. Once a person has reached a stable adult dose of sex steroid hormone therapy without significant adverse effects, the frequency of clinical visits can be reduced to one to two per year (Hembree et al, 2017)

10. We recommend that clinicians should inform and counsel all individuals seeking gender-affirming medical treatment regarding options for fertility preservation prior to initiating puberty suppression and prior to treating with hormonal therapy (97.08%) ++

Pubertal suppression and hormone treatment with sex steroid hormones may have a potential adverse effect on a person's future fertility (Cheng et al, 2019). Although some TGD people may not have given much thought to their future reproductive potential at the time of their initial assessments to start medical therapy, the potential implications of the treatment and fertility preservation options should be reviewed by the hormone prescriber and discussed with the person seeking these therapies (Ethics Committee of the American Society for Reproductive Medicine et al, 2015, De Roo et al, 2016).

Individuals with testes should be advised that prolonged treatment with estrogen often causes testicular atrophy and a reduction in sperm count and other semen parameters (Adeleye et al, 2019). Nonetheless, there are major gaps in knowledge and inconsistent findings regarding the fertility of trans feminine people who take estrogen and antiandrogens(Cheng, Pastuszak, Myers, Goodwin, & Hotaling, 2019). In one study, there was heterogeneity in testicular histology in patients who did or did not discontinue therapy prior to elective orchiectomies(Schneider et al., 2015). For example, the discontinuation of estrogen and antiandrogens for 6 weeks resulted in complete spermatogenesis for 45% of the individuals with the remainder showing meiotic arrest or spermatogonial arrest (Schneider et al., 2015). However, if serum testosterone levels within female reference ranges are confirmed, this leads to complete suppression of spermatogenesis in most transgender women (Vereecke et al. 2020). The principal fertility preservation option for trans feminine patients is sperm cryopreservation, also known as sperm banking (Mattawanon et al, 2018). For prepubertal patients, suppression of puberty with GnRH agonists pauses the maturation of sperm (Finlayson et al, 2016).

Individuals with ovaries should be advised that testosterone therapy usually results in cessation of menses and ovulation, often within a few months of initiation of therapy (Taub et al, 2020). There are also major gaps in knowledge regarding the potential effects of testosterone on oocytes and subsequent fertility of trans masculine patients(Eisenberg et al., 2020). One study found that testosterone treatment may cause polycystic ovarian morphology whereas others do not see signs of PCOS from testosterone treatment either metabolically (Chan et al) or histologically (De Roo et al.,

2017; Grynberg et al., 2010). Trans masculine patients with an intact uterus and ovaries often regain their fertility potential if testosterone therapy is discontinued(Light, Obedin-Maliver, Sevelius, & Kerns, 2014). Indeed, hormone stimulated egg retrieval from a trans masculine individual who did not discontinue testosterone therapy for assisted reproduction that resulted in a live birth has been reported (Safer and Tangpricha, 2019). Other fertility preservation options for transmasculine patients are oocyte cryopreservation and embryo cryopreservation with sperm from a partner or donor. The above options require hormonal stimulation for egg retrieval and assisted reproductive technology. For early pubertal trans youth, suppression of puberty with GnRHa pauses the maturation of germ cells, though a recent report notes that ovarian stimulation of a transgender male adolescent treated with a GnRHa in early puberty (and which was continued during ovarian stimulation) was able to result in a small number of mature oocytes that were cryopreserved(Rothenberg, Witchel, & Menke, 2019).

Initiation of Gender Affirming Hormone Therapy in Adults

11. We recommend that clinicians should evaluate and address medical conditions that can be exacerbated by lowered endogenous sex hormone concentrations and treatment with exogenous sex hormones before beginning treatment in trans and gender diverse people. (86.14%) ++

TGGD people seeking virilization must be informed on the possibilities, consequences, limitations and risks of testosterone treatment. Testosterone therapy is contraindicated during pregnancy or while attempting to become pregnant given its potential iatrogenic effects on the fetus. Relative contraindications to testosterone therapy include severe hypertension, sleep apnea and polycythemia since these conditions can be exacerbated by testosterone therapy. Monitoring of blood pressure and lipids should be performed before and after the onset of testosterone therapy. The

Commented [redacted] The explanation of this section is under-referenced and relies largely on expert opinion from endocrine society guidelines; it should be re-written as it is an important consideration in the guidelines that will likely be referenced frequently

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increase in blood pressure typically occurs within 2-4 months following the initiation of testosterone therapy (Banks K, et al in press). Patients who develop hypercholesterolemia and/or hypertriglyceridemia may need treatment with dietary modifications and/or medication. TGD people seeking feminizing treatment with a history of thromboembolic diseases such as deep vein thrombosis and pulmonary embolism should undergo evaluation and treatment prior to the initiation of hormone therapy. This is because estrogen therapy is strongly associated with increased risk of thromboembolism which cause serious harm. In addition, risk factors that can increase the risk of thromboembolic conditions should be modified such as smoking, obesity, and sedentary lifestyle. In patients with modifiable risk factors such as known thrombophilia, past history of thrombosis, or strong family history of thromboembolism, treatment with transdermal estrogen and/or concomitant treatment with anti- coagulation therapy may decrease the risk of thromboembolism; although there are limited data to guide treatment decisions. Other diseases such as hormone sensitive cancers, coronary artery disease, cerebrovascular disease, hyperprolactinemia, hypertriglyceridemia, and cholelithiasis should be evaluated prior to the initiation of estrogen therapy as these conditions can be exacerbated by estrogen. (Hembree et al., 2017)

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Commented [[redacted]: "strong" association is difficult to assess.

Greene et al have an article calculating the absolute risk as 2.3 per 1000 patient years doi 10.1373/clinchem.2018.288316

There should be a more nuanced discussion of elevated relative risk with low absolute risk

Commented [redacted] There are significant data that should be cited

Commented [redacted] Really needs citations and discussion

12. We recommend that clinicians should educate trans and gender diverse patients undergoing gender affirming treatment about the onset and time course of physical changes induced by sex hormone treatment. (96.11%) ++

The effects of testosterone treatment are multiple, and may include appearance of male-pattern body and facial hair, male pattern baldness, increased muscle mass and strength and decreased fat mass, deepening of the voice, interruption of menses (if still present), increased prevalence and severity of acne, clitoral enlargement, and higher sexual desire(Defreyne et al., 2020; Fisher et al., 2016; Giltay & Gooren, 2000; G. T'Sjoen, Arcelus, Gooren, Klink, & Tangpricha, 2019; Yeung et al., 2020) (**Table 1**). Estrogen does not alter voice or height in adult patients (Wiepes, C. et al, 2019).

The effects of estrogen treatment include induction of breast development, however, fewer than 20% reach Tanner breast stage 4-5 after 2 years of treatment. (de Blok et al, 2021). Other changes include: a decreased in testis volume, lean body mass, skin oiliness, sexual desire, spontaneous erections, facial hair, and body hair along with increased subcutaneous body fat(de Blok et al., 2020; Hembree et al., 2017; Kuper et al., 2018; Kuper et al., 2019; Taliaferro et al., 2018; Tishelman & Neumann-Mascis, 2018)Error! Bookmark not defined. (**Table 1**). Estrogen does not alter voice or height in adult patients (Iwamoto et al, 2019).

Individual components of physical change regarding time course and extent vary by individual and is related to genetics, age of initiation, and overall state of health(Deutsch, Bhakri, & Kubicek, 2015; van Dijk et al., 2019). Knowledge of the extent and timing of sex hormone–induced changes, if available, may prevent the potential harm and expense of unnecessary treatment changes, increased dosing or premature surgical procedures. (Dekker et al 2016)

Gender Affirming Hormone Regimens in Adults

13. We recommend against the use of ethinyl estradiol and conjugated estrogens in transgender women as part of a hormone affirmation regimen +++

14. We recommend the use of transdermal estrogen in transgender women who are at higher risk of VTE based on age >45 years or previous history of VTE ++

15. We suggest that clinicians should not prescribe conjugated estrogens in transgender youth and adults when estradiol is available as part of a gender affirming hormone treatment. (94%) ++

The estrogen compound and route of administration that is the most efficacious and safe in transgender women is an important topic. The recommended estrogen-

based regimens are on **Table 4**. The Free University Hospital in Amsterdam first reported 45 events of venous thromboembolism (VTE) occurring in 816 transgender women, equating to a 20-fold higher expected incidence ratio of VTE compared to a reference population(van Kesteren, Asscheman, Megens, & Gooren, 1997). Following this report, the Free University Gender Clinic recommended the use of transdermal estradiol for transgender women older than the age of 40 which subsequently lowered the incidence of VTE(Nota et al., 2019; Toorians et al., 2003). Other studies suggested that ethinyl estradiol increased clotting risk by increasing activated protein C (APC) resistance and increasing both protein C and protein S concentrations, both clotting factors (Toorians, et al, 2013). Other studies published in the past 15 years from other clinics reported lower rates of VTE in transgender women taking other forms of estrogen compared to transgender women taking ethinyl estradiol(Asscheman et al., 2013). A recent systematic review published in 2019 concluded that ethinyl estradiol was associated with the highest risk of VTE in transgender women which may also be associated with the use of progesterone(Goldstein, Khan, Reisman, & Safer, 2019).

The 2017 Endocrine Society guidelines did not recommend conjugated equine estrogens (CEE) as a treatment option because conjugated estrogens cannot be measured in the blood of transgender women which makes it difficult to prevent supraphysiologic dosing of estrogen and likely further compounds the potential risks of VTE (Hembree et al., 2017). A study from the UK, examined in a retrospective study the risks of oral CEE versus oral estradiol valerate versus oral ethinyl estradiol and found that the percentage of transgender women who had a VTE was up to 7 times higher in the oral CEE compared to transgender women on other forms of estrogen(Seal et al.,

2012). A nested case control study of over 80,000 cisgender women aged 40-79 who experienced a VTE matched to about 390,000 cisgender women without VTE found that oral estradiol had a lower risk of VTE compared to conjugated estrogens and that transdermal estrogen was not associated with increased risk of VTE(Vinogradova, Coupland, & Hippisley-Cox, 2019).

Our commissioned systematic review on different formulations of estrogen identified 2 studies that compared the risks of different formulations of estrogen in a head to head fashion. These two studies included a retrospective and cross-sectional study(Wierckx et al., 2013; Wierckx et al., 2012). There were no identified studies that evaluated the risk of different formulations of estrogen in a prospective interventional design. The retrospective study examined 214 transgender women taking transdermal estradiol (17β-estradiol gel 1.5 mg/d or estradiol patch 50 mcg/d) and daily intake of oral estrogens (estradiol 2 mg/d, estriol 2 mg/d, ethinyl estradiol 50 mcg/day, or ethinyl estradiol 30-50 mcg in an oral contraceptive)(Wierckx et al, 2013). Five percent of the cohort developed VTE, 3 (~1%) transgender women developed a myocardial infarction (MI), and 5 (~2%) transgender women developed a transient ischemic attack or cerebrovascular accident (TIA/CVA) up to a 10-year observation period. The prevalence of VTE, MI and TIA/CVA were increased after transgender women initiated on estrogen. The authors did not report differences in regimens of estrogen in these endpoints.

The cross-sectional study, conducted by the same group of investigators, examined 50 transgender women followed for 9.2 years on oral estrogen (estradiol valerate 2mg/d, estriol 2 mg/d or ethinyl estradiol 50-120 mcg/day) and on transdermal

estradiol (17β-estradiol 1.5 mg/day or estradiol 50 mcg/day) (Wierckx et al, 2012). Twelve percent (6 out of 50) developed either a VTE, MI, or TIA/CVA. Two of the participants were taking conjugated estrogen 0.625 mg/d (with one in combination with cyproterone acetate), 2 participants were taking ethinyl estradiol 20-50 mcg/d, 1 was taking cyproterone acetate 50 mg/d, and the sixth participant did not have the estrogen regimen defined. None of the subjects taking oral estradiol or transdermal estradiol developed a VTE, MI, or TIA/CVA.

One prospective study examined the route of estrogen administration in 53 transgender women in a multi-center study throughout Europe. Transgender women younger than the age of 45 years (n=40) received estradiol valerate 4 mg/d in combination with cyproterone acetate (CPA) 50 mg/d and transgender women older than 45 years (n=13) received transdermal 17β-estradiol also with CPA. No VTE, MI, or TIA/CVA was reported after 1 year of follow-up in either the oral or transdermal estrogen group. An additional retrospective study from Vienna found no occurrences of VTE among 162 transgender women on transdermal estradiol followed for a mean of 5 years(Ott, Kaufmann, Bentz, Huber, & Tempfer, 2010).

We are strongly confident in our recommendation against the use of ethinyl estradiol based on historical data from the Amsterdam clinic demonstrating a reduction of VTE after discontinuing the use of ethinyl estradiol and the recent systematic review demonstrating increased risk of VTE in transgender women on ethinyl estradiol(Weinand & Safer, 2015) We are confident in our recommendation against the use of CEE based on the study by Seal et al, 2012 demonstrating an increased risk of VTE in transgender women taking CEE compared to other formulations of estrogen and

data from cisgender women on hormone replacement therapy(Canonico et al., 2007; Seal et al., 2012). Prospective and retrospective studies in transgender women report VTE/MI/CVA only in those taking CEE or ethinyl estradiol. Since estradiol is inexpensive, more widely available, and appears safer than CCE in limited studies, the committee recommends against using CEE when estradiol is an available treatment option. The quality of studies may be limited to prospective cohort or cross-sectional study designs; however, the evidence is consistent that ethinyl estradiol and CEE are associated with more risk of VTE/MI/CVA in transgender women leading to the committee's stronger level of recommendation.

We are also confident in our recommendation for the use of transdermal preparations of estrogen in older transgender women (age >45 years) or with previous history of VTE. The confidence in our recommendation comes from the decreased in VTE incidence from the Amsterdam clinic when switching transgender women to transdermal preparations after age 40. Furthermore, the prospective multi-center cohort study ENIGI found no VTE/MI/CVA in transgender women who are routinely switched to transdermal estrogen at age 45 and from the study by Ott et al demonstrating no VTE in 162 transgender women treated with estradiol patches(Ott et al., 2010, Wierckx et al, 2014).

16. We recommend that clinicians prescribe testosterone lowering medications (either cyproterone acetate, spironolactone or GnRH agonist) for transgender youth and adults with testes taking estrogen as part of a hormone treatment plan if their individual goal is to approximate circulating sex hormone concentrations of cisgender women. (88%) +++

Most gender clinics in the United States and Europe prescribe estrogen combined with a testosterone lowering medication(Mamoojee, Seal, & Quinton, 2017) (**Table 5).** In the United States, spironolactone is the most commonly prescribed testosterone lowering medication. In the UK, GnRHa are commonly used as the testosterone lowering medication. In the rest of Europe, cyproterone acetate is used. The rationale for adding a testosterone lowering medication is two-fold: 1. To lower the testosterone levels into the cisgender female reference range and, 2. To lower the amount of estrogen needed to produce adequate physical effects. Each testosterone lowering medication has a different side effect profile. Spironolactone is an anti-hypertensive and potassium sparing diuretic and thus may cause hyperkalemia, increased frequency of urination and lower blood pressure. (ref?) Cyproterone acetate has been associated with reports of meningioma and hyperprolactinemia(Nota et al., 2018). GnRH agonists are very effective in lowering testosterone levels and could result in osteoporosis if insufficient doses of estrogen are given concurrently (Klink et al, 2014).

One systematic review on this topic identified only 1 study that compared different testosterone lowering medications in a head to head design (cyproterone acetate vs leuprolide)(Gava et al., 2016). There were two studies that compared testosterone lowering medications versus no testosterone lowering medication in transgender women on estrogen. This systematic review did not provide sufficient evidence to recommend one of the three testosterone lowering medications in terms of better safety on bone outcomes, testosterone levels, potassium levels, or incidence of hyperprolactinemia or meningiomas (Wilson et al., 2020). However, the review did

Commented [redacted]: Is this from the same publication? There are definitely sources for prevalence of antiandrogens in different areas

https://doi.org/10.1111/cen.14329

Commented [redacted]: this is not an evidence-based assertion; it was included in endocrine society guidelines without evidence, and there are no data measuring "efficacy" of transition with and without antiandrogens. Regardless, it does not meet the +++ rating of the recommendation; perhaps downgrade to ++ if this is the rationale?

report that spironolactone based regimens increased prolactin levels up to 45% whereas cyproterone based regimens increased prolactin levels by over 100%. However, the clinical significance of elevated prolactin levels is not quite clear as the rates of prolactinomas are not significantly elevated in either groups taking spironolactone or CPA (Wilson et al., 2020). One retrospective cohort study from the United States reported that about 100 transgender women taking estrogen plus spironolactone treated at a single center did not have any clinically significant increases in prolactin levels (Bisson, Chan, & Safer, 2018). A retrospective study from the Netherlands of 2,555 transgender women taking primarily CPA with various formulations of estrogen reported increased standardized incidence ratio of meningiomas in patients who used cyproterone acetate after gonadectomy for many years compared to the general Dutch population(Nota et al., 2018). Furthermore, in a shorter study in the Netherlands, 107 transgender women had transient elevations in prolactin levels following treatment with cyproterone acetate which declined to normal after discontinuation of the cyproterone acetate(Defreyne et al., 2017). A recent publication not included in the systematic review examined 126 transgender women on spironolactone, GnRHa or cyproterone and concluded that cyproterone use was associated with higher prolactin levels and worse lipid profile than spironolactone use or GnRHa use (Sofer et al., 2020). The committee decided not to make a recommendation for or against monitoring prolactin levels at this time, balancing the costs and accessibility of the measurement against the clinical significance of an elevated prolactin level. Clinicians need to make individualized clinical decisions based the type

of hormone regimen and/or symptoms of hyperprolactinemia (e.g. galactorrhea, visual field changes) on the necessity to measure prolactin levels.

Cyproterone has also been linked to meningiomas. Nine cases of meningioma have been reported in the literature among transgender women primarily taking cyproterone acetate(Mancini et al., 2018). This increased risk is also noticed in cisgender populations. In 2020, the European Medicines Agency published a report recommending that cyproterone products with daily doses of 10 mg or more should be restricted because of a risk of developing meningioma (European Medicines Agency). Most likely this association with an increased risk is a specific effect of cyproterone acetate and is not found for the other testosterone lowering drugs. In the United States where cyproterone acetate is not available, the North American Association of Central Cancer Registries (NAACCR) database did not demonstrate an increased risk of brain tumors (not specific to meningiomas) among transgender women(Nash et al., 2018). Furthermore, in the Kaiser cohort of 2,791 transgender women, there was not an increased hazard ratio of brain tumors compared to cisgender controls(Silverberg et al., 2017). There have not been any long-term studies that have reported on the risk of meningiomas and prolactinomas in transgender women taking GnRH agonists.

Our strong recommendation for testosterone lowering medication part of a hormone regimen for transgender individuals with testes based on the global practice of using these medications in addition to estrogen therapies and the relatively minimal risk with these therapies. However, we are not able to make a recommendation that favors one testosterone lowering medication over another at this time. The published data thus far raises some concerns about cyproterone acetate in causing meningiomas when

used for a long time (>2 years) and higher doses (>10mg daily). (Weill, A., et al, 2021, Nota, N., et al, 2018, Ter Wengel, P. et al, 2016)

17. We recommend that clinicians should monitor hematocrit (or hemoglobin) in transgender youth and adults treated with testosterone. (96%) +++

There are good quality data for a rise in hematocrit (or hemoglobin) associated with testosterone treatment in transgender persons(Defreyne et al., 2018, Antun et al, 2020). The testosterone regimens in the systematic review included testosterone esters ranging from the equivalent of 25- 250 mg SC/IM weekly, testosterone undecanoate 1000 mg every 12 weeks, or testosterone gel 50 mg to skin daily(Defreyne et al., 2018; Gava et al., 2018; Giltay, Gooren, Emeis, Kooistra, & Stehouwer, 2000; Meriggiola et al., 2008; Pelusi et al., 2014; G. G. T'Sjoen et al., 2005; Wierckx, Van Caenegem, et al., 2014; Wierckx, Van de Peer, et al., 2014) . The expected rise should be consistent with cisgender male reference ranges.

Preparation for Gender Affirming Surgeries in Youth and Adults

18. We suggest that clinicians should collaborate with surgeons regarding hormone use before and after gender affirming surgery. (82.96%) ++

19. We suggest that clinicians should counsel patients on the various options for genital gender-affirming surgery on trans and gender diverse patients, unless surgery is not desired or medically contraindicated. (78.65%) ++

Despite the absence of evidence, perioperative clinical standards for gender affirming surgeries have included cessation for hormone therapy for 1-4 weeks before and after gender affirming surgeries, most commonly with regard to genital

surgeries(Hembree et al., 2017, Gaither et al., 2018). Such practice was meant to mitigate the venous thromboembolic (VTE) risk associated with exogenous estrogen therapy(Hembree et al., 2017). Estrogen and testosterone could be resumed at some period post-operatively

When carefully examined, investigators have found no peri-operative increase in VTE risk among transgender individuals relative undergoing surgery who were maintained on sex steroid treatment throughout relative to rates of VTE for patients who had sex steroid treatment cessation pre-operatively (Kozota, 2021). Sex steroid treatment is especially important after gonadectomy, to avoid sequelae of hypogonadism, including osteoporosis as well as to maintain mental health and quality of life (Fisher et al., 2016; Rosen et al., 2019). Thus, hormone providers and surgeons should educate patients on the necessity of continuous exogenous hormone therapy after gonadectomy.

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In order to inform patients and to serve as clinical advocates, clinicians should be knowledgeable regarding the risks/benefits of gender-affirming surgeries along with the performance measures and surgical outcomes of the surgeons to whom they might refer (Beek, Kreukels, Cohen-Kettenis, & Steensma, 2015; Colebunders, Brondeel, D'Arpa, Hoebeke, & Monstrey, 2017; Wiepjes et al., 2018, Tangpricha & Safer, 2019). In general, most surgeries can be thought of in three regions: the face, chest/breasts, and genitalia (internal and external). Additional procedures include body contouring and voice surgery.

Facial affirming surgery includes multiple options including, but not limited to chondrolanryngoplasty, rhinoplasty, contouring or augmentation of the jaw, chin, and

forehead, facelift, and hair transplantation. Chest/breast surgery options include breast augmentation, double mastectomy with nipple grafts, periareolar mastectomy, and liposuction. The most common gender affirming surgery for trans masculine individuals is masculinizing chest surgery (mastectomy)(Horbach et al., 2015; Kailas, Lu, Rothman, & Safer, 2017).

Internal genital surgery options include orchiectomy, hysterectomy, salpingo-oophorectomy, vaginoplasty, and colpectomy/vaginectomy(Horbach et al., 2015; Jiang, Witten, Berli, & Dugi, 2018). The inner lining in vaginoplasty is typically made with penile skin, skin grafts, a combination of both or a bowel segment. Removal of uterus/ovaries can be done individually or all at once (hysterectomy, salpingo-oophorectomy and colpectomy). If a colpectomy is performed, a hysterectomy must also be performed. The ovaries may remain in situ, upon patient request. A potential benefit of leaving one or both ovaries is fertility preservation and a potential risk include presence of ovarian cancer risk (De Roo et al, 2017)

External genital surgery options include vulvoplasty, metoidioplasty and phalloplasty(Djordjevic et al., 2008; Frey, Poudrier, Chiodo, & Hazen, 2016). Hair removal can be necessary before external genital procedures (Marks et al, 2019). Vulvoplasty can include the creation of the mons, labia, clitoris, and urethral opening. Urethral lengthening is an option for both metoidioplasty and phalloplasty but is associated with a greatly increased complication rate(Schechter & Safa, 2018). Wound care and physical therapy are necessary for resulting wounds from the donor sites for phalloplasty (van Caenegam et al, 2013). Pelvic physical therapy can be an important adjunct intervention after surgery for voiding and sexual function (Jiang et al, 2019).

Dialogue and good understanding, with communication in a common language among patients, clinicians and surgeons will contribute to well-considered choices about surgical options.

20. We recommend that clinicians should initiate and continue gender-affirming hormone therapy in transgender youth and adults who wish this treatment due to demonstrated improvement of psychosocial functioning and quality of life. (88%) +++

21. We recommend that, unless contraindicated, clinicians should maintain existing hormone therapy if TGGD individual's mental health deteriorates, and assess the reason for the deterioration. (89%) ++

Several mental health disparities have been documented in the transgender population including depression, suicidality, anxiety, decreased self-esteem, and post-traumatic stress disorder (Becerra-Culqui et al, 2018; Eisenberg et al., 2017; Heylens et al, 2014). The gender minority stress model provides evidence of several mediators and moderators of these disparities(Hendricks & Testa, 2012). Mediators and moderators of mental health disparities unique to transgender people include experiences of discrimination, victimization, misgendering, family rejection, and internalized transphobia (Goldblum et al., 2012; Russell et al., 2018; Testa et al., 2012). Factors that have a positive effect on mental health include family acceptance, supportive social and romantic relationships, trans community connectedness, trans identity pride, affirming and inclusive policies, having updated legal name/gender documentation, and physical gender transition based on individualized embodiment goals (Bauer et al., 2015; Bockting et al., 2013; de Vries et al., 2014; Du Bois et al., 2018; Gower et al., 2018;

Hendricks & Testa, 2012; Keo-Meier et al., 2015; Meier et al., 2013; Pflum et al., 2015; Smith et al., 2018; Ryan et al., 2010).

Hormone therapy has been found to have a direct positive impact on the mental health and quality of life of transgender youth and adults who desire this treatment (Allen, Watson, Egan, & Moser, 2019; Bauer, Scheim, Pyne, Travers, & Hammond, 2015; Russell, Pollitt, Li, & Grossman, 2018; Ryan, 2009). In many cases, hormone therapy is considered a lifesaving intervention (Allen et al., 2019; Grossman & d'Augelli, 2006; Moody et al., 2015). Several studies have found associations between the initiation of hormone therapy improved mental health in youth and adults (Colizzi et al., 2013; Colizzi et al., 2014; Costa, Carmichael, & Colizzi, 2016; A. L. de Vries et al., 2014; Fisher et al., 2016; Kuper, Stewart, Preston, Lau, & Lopez, 2020; Nguyen et al., 2018; Tucker et al., 2018; White Hughto & Reisner, 2016) including improvements in quality of life (Gorin-Lazard et al., 2012; Gorin-Lazard et al., 2013; Murad et al., 2010; Newfield, Hart, Dibble, & Kohler, 2006; White Hughto & Reisner, 2016), decreased anxiety and depression (Colizzi, Costa, & Todarello, 2014; Davis & Meier, 2014; de Vries, Doreleijers, Steensma, & Cohen-Kettenis, 2011; Gómez-Gil et al., 2012; Rowniak, Bolt, & Sharifi, 2019; Keo-Meier et al., 2015), decreased stress (Meier, Fitzgerald, Pardo, & Babcock, 2011), and decreased paranoia (Keo-Meier et al., 2015). A prospective controlled trial using the MMPI-2, demonstrated significant improvement in multiple domains of psychological functioning in transgender men after only 3 months of testosterone (Keo-Meier et al., 2015). Although there are higher rates of autism symptoms in the transgender population, these symptoms have not been found to

increase after initiation of hormone therapy (Nobili, Glazebrook, Bouman, Baron-Cohen, & Arcelus, 2020).

Because reductions in depression symptoms may correlate with reduced suicide risk, withholding hormone therapy based on depression or suicidality may cause harm (Allen, Watson, Egan, & Moser, 2019; Keo-Meier et al., 2015; Levy, Crown, & Reid, 2003). Turban (2020) found decreased odds of lifetime suicidal ideation in adolescents who desired pubertal suppression and had access to this treatment compared to those who desired it and did not have access (Turban, King, Carswell, & Keuroghlian, 2020). A recent systematic review found that pubertal suppression in TGD adolescents was associated with improved social life, decreased suicidality in adulthood, improved psychological functioning and quality of life (Rew et al, 2020). As evidence suggests that hormone therapy directly decreases symptoms of depression and anxiety, the practice of withholding hormone therapy until these symptoms are treated with traditional psychiatric treatment is thought to be iatrogenic (Keo-Meier et al., 2015). If psychiatric treatment is indicated, it can be started or adjusted concurrently without discontinuing hormone therapy.

Table 1 Expected Time Course of Physical Changes in Response to Gender Affirming Hormone Therapy

Testosterone Based Regimen

Effect	Onset	Maximum
Skin Oilness/acne	1-6 mo	1-2 y
Facial/body hair growth	6-12 mo	>5 y
Scalp hair loss	6-12 mo	>5 y
Increased muscle mass/strength	6-12 mo	2-5 y
Fat redistribution	1-6 mo	2-5 y
Cessation of menses	1-6 mo	1-2 y
Clitoral enlargement	1-6 mo	1-2 y
Vaginal atrophy	1-6 mo	1-2 y
Deepening of voice	1-6 mo	1-2 y

Estrogen and Testosterone Lowering Based Regimen

Effect	Onset	Maximum
Redistribution of body fat	3-6 mo	2-5 y
Decrease in muscle mass and strength	3-6 mo	1-2 y
Softening of skin/decreased oiliness	3-6 mo	Unknown
Decreased sexual desire	1-3 mo	Unknown
Decreased spontaneous erections	1-3 mo	3-6 mo
Decreased sperm production	Unknown	2 years
Breast growth	3-6 mo	2-5 y
Decreased testicular volume	3-6 mo	Variable
Decreased terminal hair growth	6-12 mo	>3y
Increased scalp hair	Variable	Variable
Voice changes	Minimal	

Data for Testosterone based regimens from (Ahmad & Leinung, 2017; Irwig, Childs, & Hancock, 2017; Klaver et al., 2018; Park, Carter, & Larson, 2019; Schönauer et al., 2020; Stoffers, de Vries, & Hannema, 2019; Taub et al., 2020; Van Caenegem et al., 2015; Yeung et al., 2020)
Data for Estrogen and Testosterone lowering based regimen from (de Blok et al., 2018; Irwing 2017; Matoso et al., 2018; Reisman, Goldstein, & Safer, 2019; Stevenson, Wixon, & Safer, 2016, Wierckx et al, 2012)

TABLE 2 RISKS ASSOCIATED WITH SEX STEROID HORMONE THERAPY, BOLDED ITEMS ARE CLINICALLY SIGNIFICANT (Updated from SOC7)

RISK LEVEL	Estrogen based regimens	Testosterone based regimens
Likely increased risk	**Venous Thromboembolism** **Infertility** **Hyperkalemia**[s] Hypertrigyceridemia Weight Gain	**Polycythemia** **Infertility** Acne Androgenic alopecia Sleep Apnea Weight Gain Decreased HDL cholesterol and increased LDL cholesterol
Likely increased risk with presence of additional risk factors	Cardiovascular Disease Cerebrovascular Disease Meningioma [c] Polyuria/dehydration [s] Cholelithiasis	Hypertriglyceridemia
Possible increased risk	Hypertension Erectile dysfunction	Hypertension
Possible increased risk with presence of additional risk factors	Type 2 Diabetes Low bone mass/osteoporosis Hyperprolactinemia	Type 2 Diabetes Cardiovascular Disease
No increased risk or inconclusive	Breast and Prostate Cancer	Low bone mass/osteoporosis Breast, Cervical, Ovarian, Uterine cancer

[C] cyproterone based regimen
[S] spironolactone based regimen

TABLE 3 GENDER AFFIRMING HORMONE REGIMENS IN TRANSGENDER AND GENDER DIVERSE YOUTH (Adapted from the Endocrine Society Guidelines)

Induction of female puberty with oral 17ß-estradiol
Initiate at 5µg/kg/d and increase every 6 mo by 5 µg/kg/d up to 20 µg/kg/d according to estradiol levels
Adult dose = 2 – 6 mg/day

In post-pubertal transgender adolescents, the dose of 17ß-estradiol can be increased more rapidly:
1 mg/d for 6 mo followed by 2 mg/d and up according to estradiol levels

Induction of female puberty with transdermal 17ß-estradiol
Initial dose 6.25-12.5 µg/24 h (cutting 24 g patch to ¼ then ½)
Titrate up by every 6 mo by 12.5 µg/24 h according to estradiol levels
Adult dose = 50-200 µg/24 h
For alternatives once at adult dose, see Table 4

Induction of male puberty with testosterone esters
25 mg/m^2/2 wk (or alternatively half this dose week)
Increase by 25 mg/m^2/2 wk every 6 mo until adult dose and target testosterone levels achieved. See alternatives for testosterones (Table 4)

TABLE 4 HORMONE REGIMENS IN TRANSGENDER AND GENDER DIVERSE ADULTS*

Transgender Females	
Estrogen	
Oral	
Estradiol	2.0 – 6.0 mg/day
Transdermal	
Estradiol transdermal patch	0.025 – 0.2 mg/day
Estradiol gel various	‡ daily to skin
Parenteral	
Estradiol valerate or cypionate	5-30 mg IM every 2 weeks
	2-10 IM every week
Anti-Androgens	
Spironolactone	100 – 400 mg/day
Cyproterone acetate	10 mg/day
GnRH agonist	3.75- 7.50 mg SQ monthly
GnRH agonist depot formulation	11.25/22.5 mg SQ 3/6 monthly

‡ Amount applied varies to formulation and strength

Transgender males	
Testosterone	
Parenteral	
Testosterone enanthate/cypionate	50 - 100 IM/SQ weekly or
	100 – 200 IM every weeks
Testosterone undecanoate	1000 mg IM every 12 weeks
Transdermal testosterone	
Testosterone gel 1.6%	50-100 mg/day
Testosterone transdermal patch	2.5 – 7.5 mg/day

**Doses are titrated up or down until sex steroid hormone levels are in the therapeutic range*

Table 5 Hormone Monitoring of Transgender and Gender Diverse People on Gender Affirming Hormone Therapy (adapted from the Endocrine Society Guidelines)

Transgender Male

1. Evaluate patient approximately 3 mo (with dose changes) in the first year and one to two times per year to monitor for appropriate physical changes in response to testosterone.
2. Measure serum total testosterone every 3 mo (with dose changes) until levels are in the range of reference men.
    a. For parenteral testosterone, the serum total testosterone should be measured midway between injections. The target level is 400-700 ng/dL. Alternatively, measure peak and trough peaks to ensure levels remain the range of reference men.
    b. For parenteral testosterone undecanoate, testosterone should be measured just before injection. If the level is <400 ng/dL, adjust the dosing interval
    c. For transdermal testosterone, the testosterone level can be measured no sooner than after 1 wk of daily application (at least 2 hr after application of product)
3. Measure hematocrit or hemoglobin at baseline and approximately 3 mo (with dose changes) for the first year and then one to two times a year.
4. Follow primary care screening per primary care chapter recommendations

Transgender Female

1. Evaluate patient approximately every 3 mo (with dose changes) in the first year and one to two times per year to monitor for appropriate physical changes in response to estrogen.
    a. Serum testosterone levels should be less than 50 ng/dL
    b. Serum estradiol should be in the range of 100-200 pg/mL
2. For individuals on spironolactone, serum electrolytes, particularly potassium, and kidney function, particularly creatinine, should be monitored.
3. Follow primary care screening per primary care chapter recommendations

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RE: [External] Re: question for the surgeons

From: [redacted]
To:
Cc:
Date: Wed, 06 Oct 2021 10:29:43 -0400
Attachments: Grfit (2020) Timing of Puberty Suppression and Surgical Options for Transgender Youth_Pediatrics.pdf (1.06 MB); Bouman (2016) Total laparoscopic sigmoid vaginoplasty.pdf (64.82 kB)

We have one paper that states that surgical consequences of puberty suppression should be discussed at the time of start suppression.
So yes, it should be part of informed consent, the pro and cons.

We do colon vagina's with good results, so here in the Netherlands it seems not such a big worry.

[redacted]

Van: [redacted]
Verzonden: woensdag 6 oktober 2021 15:01
Aan: [redacted]
CC: [redacted]
Onderwerp: Re: [External] Re: question for the surgeons

There isn't much published data on this topic. I don't think there is a one size fits all. I think informed consent is the way to go in terms of weighing the risks of early pubertal blockage vs amount of surgical material needed for vaginoplasty. Maybe this is an opportunity for additional advances in the surgical field?

[redacted]

[redacted]

From: [redacted]
Sent: Wednesday, October 6, 2021 8:56 AM
To: [redacted]
Cc: [redacted]
Subject: [External] Re: question for the surgeons

This is something that [redacted] mentioned in the Gothenburg meeting and then she spoke to you [redacted] about it too, I believe. It will make sense if is not there to add information which will be clinical more than academic regarding the effect of starting on blockers in early puberty on the type of surgery for vaginoplasty that they will be able to have in the future with more possible complications from it (if using the colom), but of course not every tranwoman wishes vaginoplasty

[redacted]

From: [redacted]
Sent: Wednesday, October 6, 2021 2:49:43 PM

To [redacted]
Cc: [redacted]

Subject: Re: question for the surgeons

I think so. I don't know what the evidence base is for this - but it seems that there is a concern and might need to be part of informed consent.

On Wed, Oct 6, 2021 at 7:41 AM [redacted] wrote:

> Thank you. Do you think it is important to address?
>
> Sent from my iPhone
>
> > On Oct 6, 2021, at 8:32 AM, [redacted] wrote:
> >
> > Hello [redacted]
> >
> > I have seen the article (and spoken with [redacted]
> >
> > We do not specifically address the impact of gnrh agonists on surgery. We do discuss the multidisciplinary approach when considering surgery on adolescents
> >
> > Thanks
> >
> > [redacted]
> >
> > Sent from my iPhone
> >
> > > On Oct 6, 2021, at 6:53 AM, [redacted] wrote:
> > >
> > > Hi all,
> > >
> > > Something tells me we are all aware of this article:
> > > https://bariweiss.substack.com/p/top-trans-doctors-blow-the-whistle
> > >
> > > In it, there are concerns about the surgical implications of blockers from WPATH leadership, and this has made its way across the airwaves with responses indicating that the SOC is addressing this issue. However, this is something that we currently do **not** address in our chapter since there's no specific research article to cite on the subject. That being said, it's a rather large point of discussion, and I believe it's an unavoidable subject that really does need to be addressed. Personally I think that discussing the hypothetical risks of blockers, including the potential effect on surgical outcomes and sexual health, is something that should be mentioned when getting consent from parents/caregivers for use of blockers. I know that I do this when working with families and it is greatly appreciated by families.
> > >
> > > Not having seen the surgery chapter, I want to double check if it is in that chapter. If not, how do we envision SOC addressing this- in the Adol chapter?

Thanks all,

[redacted]

--

Re: [External] Final Chapter Edits Ready for Review - SOC8 Hormone Chapter

From: [redacted]
To: [redacted]
Cc: [redacted]
Date: Fri, 29 Oct 2021 05:48:55 -0400

Thanks [redacted]
I feel for you having to do the exam…it is a crazy system…hope it went well.

If you think your chapter members are going to make changes or suggestions is better they do that now than creating another draft, so I suggest you send it to them so they can feedback within 1 week and send us a clean final copy to us in a week time, what do you think?

This is a question for [redacted] I noticed that your chapters says:. "**Statements supported by systematic literature reviews are rated as follows: ++++ strong certainty of evidence, +++ moderate certainty of evidence, ++ low certainty of evidence, + very low certainty of evidence".**

My understanding was that we were not going to make a difference between statements based on LR and the rest, is that right [redacted]? If so, we will need to remove the +, ++, +++, ++++

Regards
[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

From: [redacted]
Date: Thursday, 28 October 2021 at 20:04
To: [redacted]
[redacted]
Cc: [redacted]
[redacted]
Subject: Re: [External] Final Chapter Edits Ready for Review - SOC8 Hormone Chapter

Dear All,
Please see the attached SOC Hormone chapter. There were quite a number of tasks that needed to be done so I needed the extra week. I have accepted most of the edits. I have added references. I have put in [redacted] additional comment about the discussion regarding surgical options for early pubertal children on blockers. There are a couple of comments that I could not address since [redacted] wanted an expansion of one of our statements. I don't think it is necessary to add more text since the statement really refers to statements that should be in the primary care chapter. If you agree that we don't need to add anymore text to our chapter, then I have completed all of the requested work by the reference/copy editor. Please let me know if there is anything else at this stage. I know that some of our chapter members want to read this again. It might be a good idea given all of the edits but I assume there will be an opportunity in the future as this moves along to completion.
Sincerely,
[redacted]

[redacted]

[redacted]

From: [redacted]
Sent: Friday, October 8, 2021 3:27 AM
To: [redacted]
Cc: [redacted]
Subject: Re: [External] Final Chapter Edits Ready for Review - SOC8 Hormone Chapter

Hi [redacted]
Please Agree or decline the edits and add in the text anything else that is needed and send us a clean copy. That will be the final copy then.
Regards
[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

From: [redacted]
Sent: 07 October 2021 9:09 PM
To: [redacted]; HormoneSOC8 <HormoneSOC8@wpath.org>
Cc: [redacted]
Subject: Re: [External] Final Chapter Edits Ready for Review - SOC8 Hormone Chapter

This is great. What is the most efficient way to provide information? Do you want me to add more comments or just accept the comments/changes that I agree with? Overall I agree with the copyedits and can answer the few queries.

[redacted]

[redacted]

[redacted]

From: [redacted]
Sent: Thursday, October 7, 2021 2:45 PM
To: [redacted] HormoneSOC8 <HormoneSOC8@wpath.org>
Cc: [redacted]
Subject: [External] Final Chapter Edits Ready for Review - SOC8 Hormone Chapter

Dear [redacted] and all,

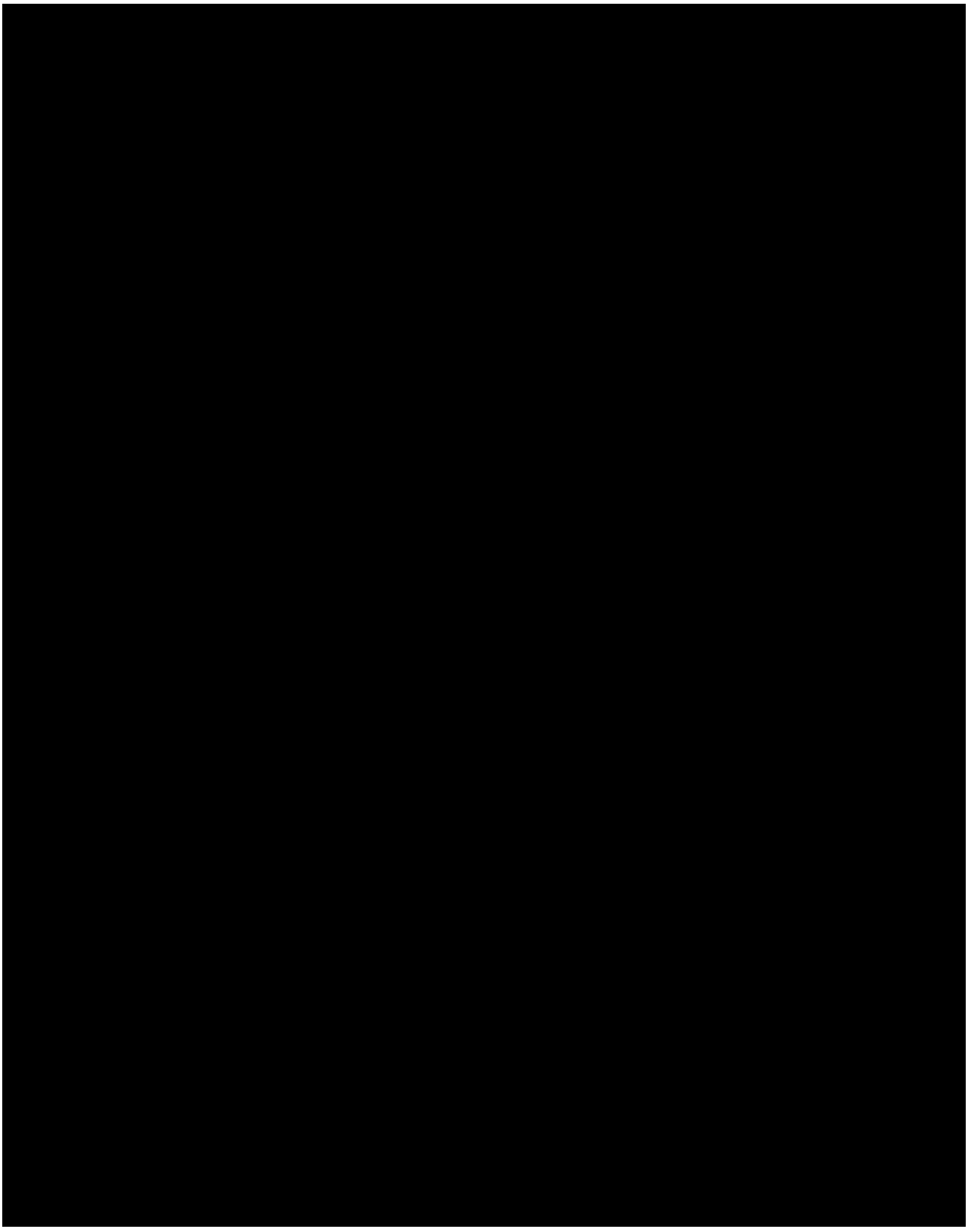
I hope this email finds you well. Please see attached for the feedback from the SOC8 Copyeditor and Reference Checker for the SOC8 Hormone Chapter. Please review the edits and comments throughout the document and advise any issues/concerns **within 2 weeks (by EOD Thursday, October 21, 2021**), so this chapter can be finalized.

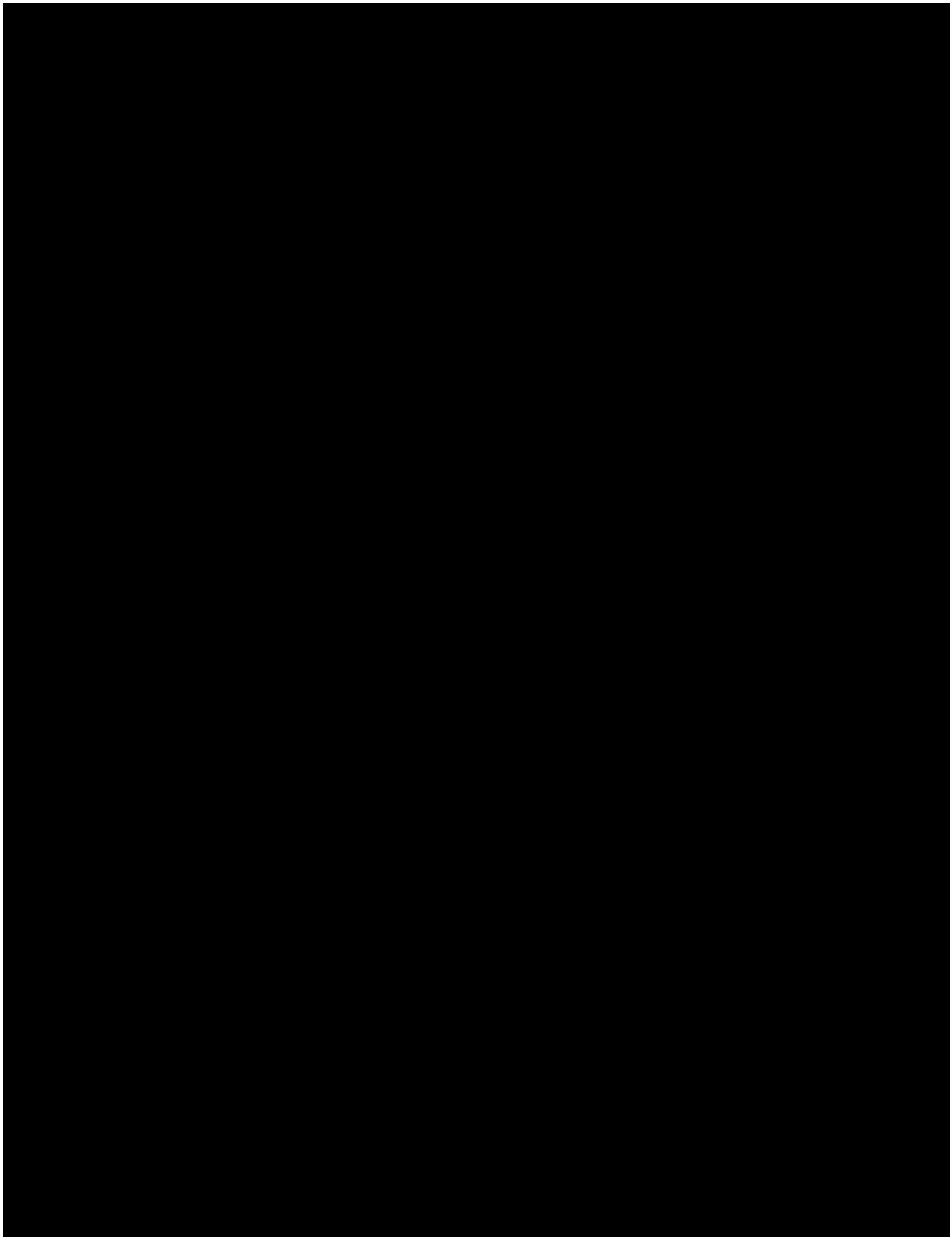
Please let us know if you have any questions.

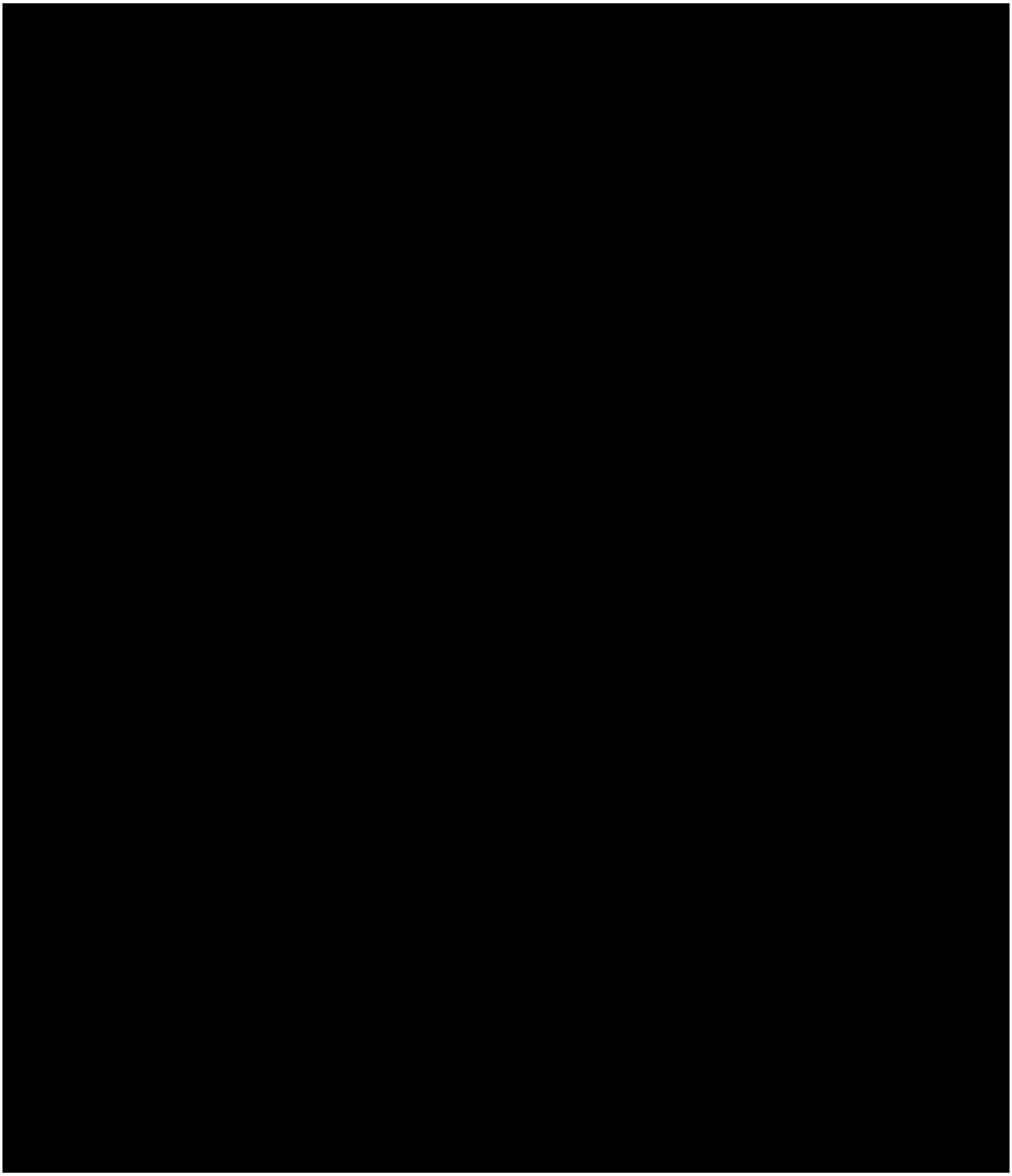
All best,
[redacted]

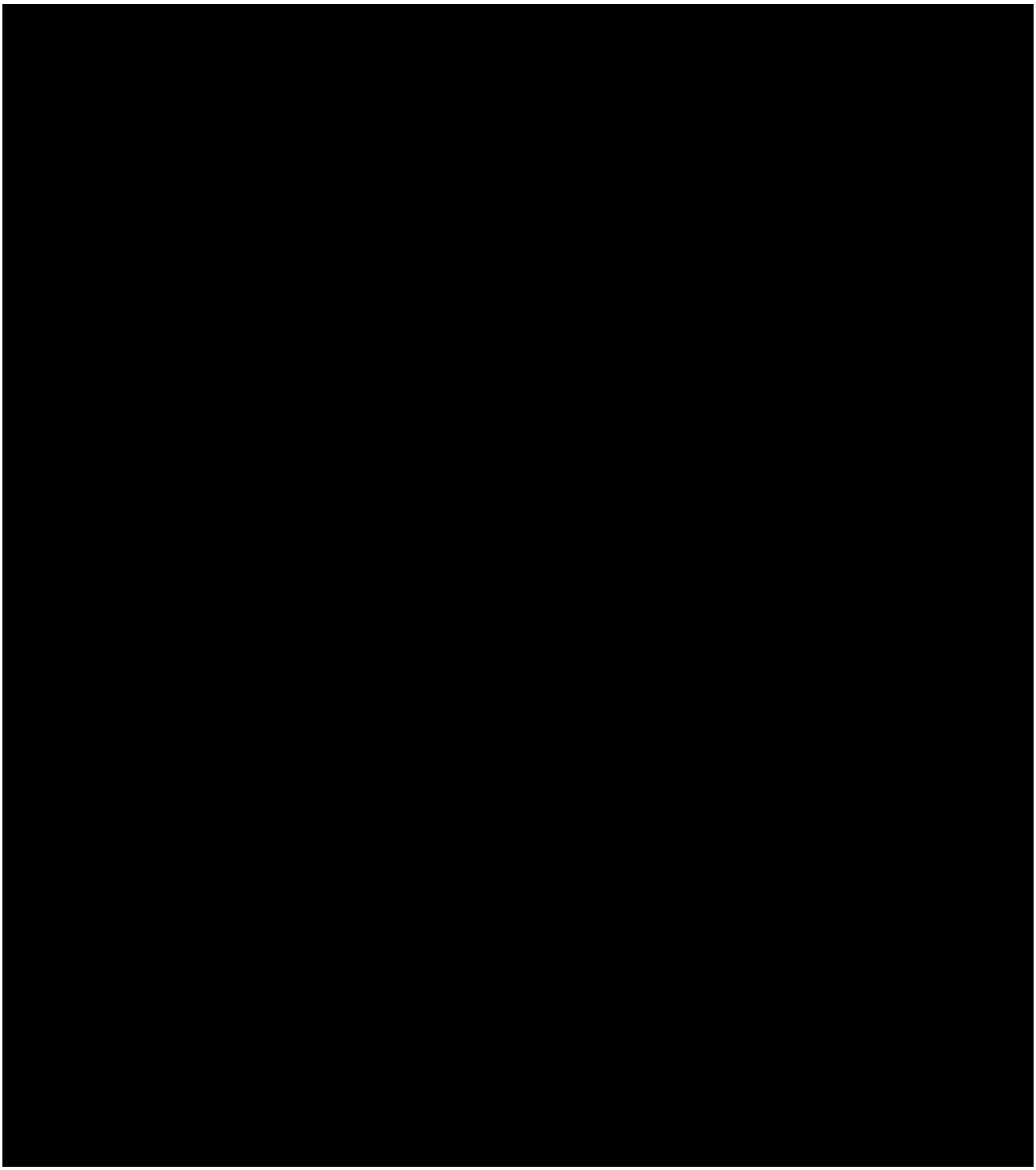
This message and any attachment are intended solely for the addressee and may contain confidential information. If you have received this message in error, please contact the sender and delete the email and attachment.

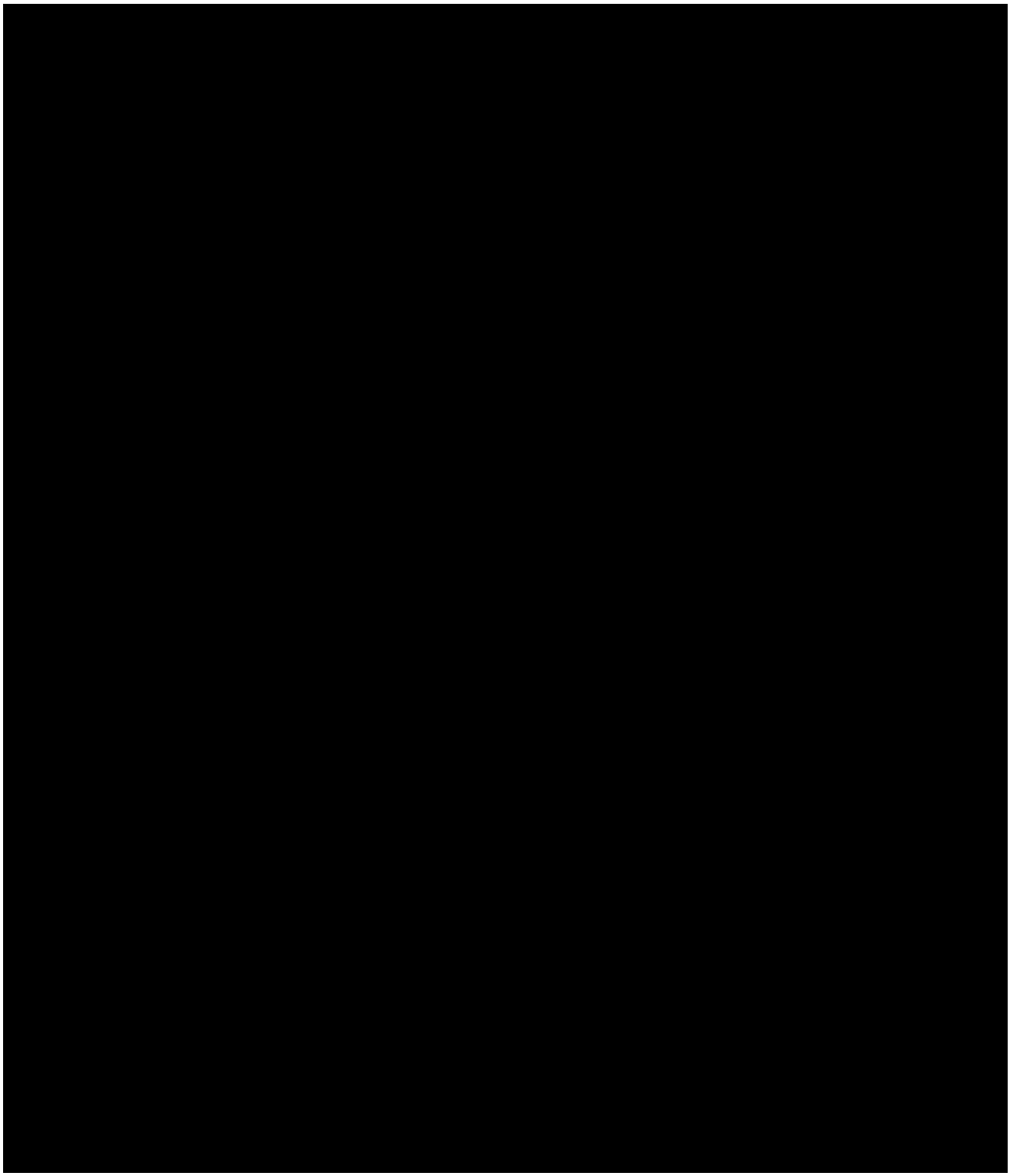
Any views or opinions expressed by the author of this email do not necessarily reflect the views of the University of Nottingham. Email communications with the University of Nottingham may be monitored where permitted by law.

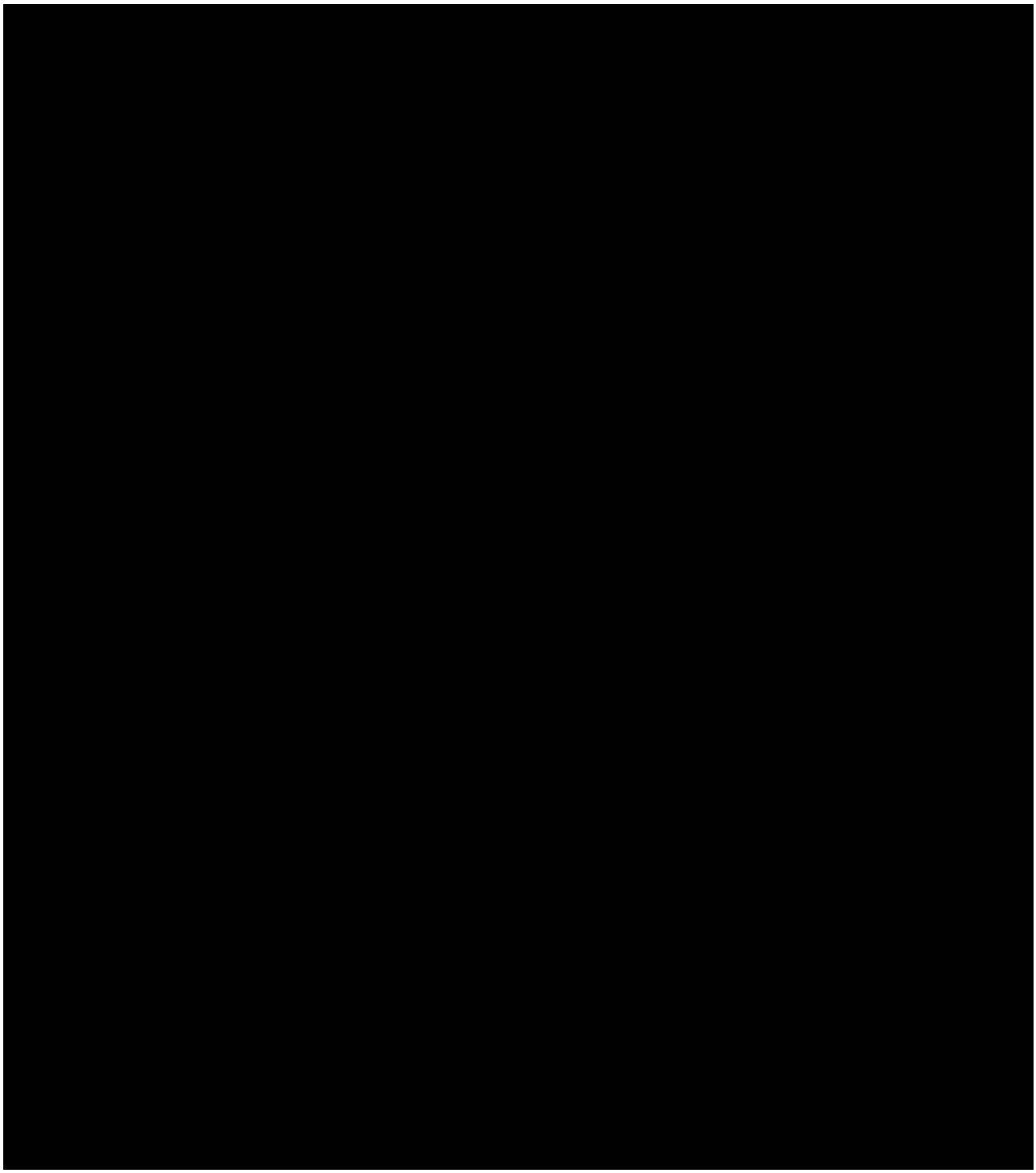


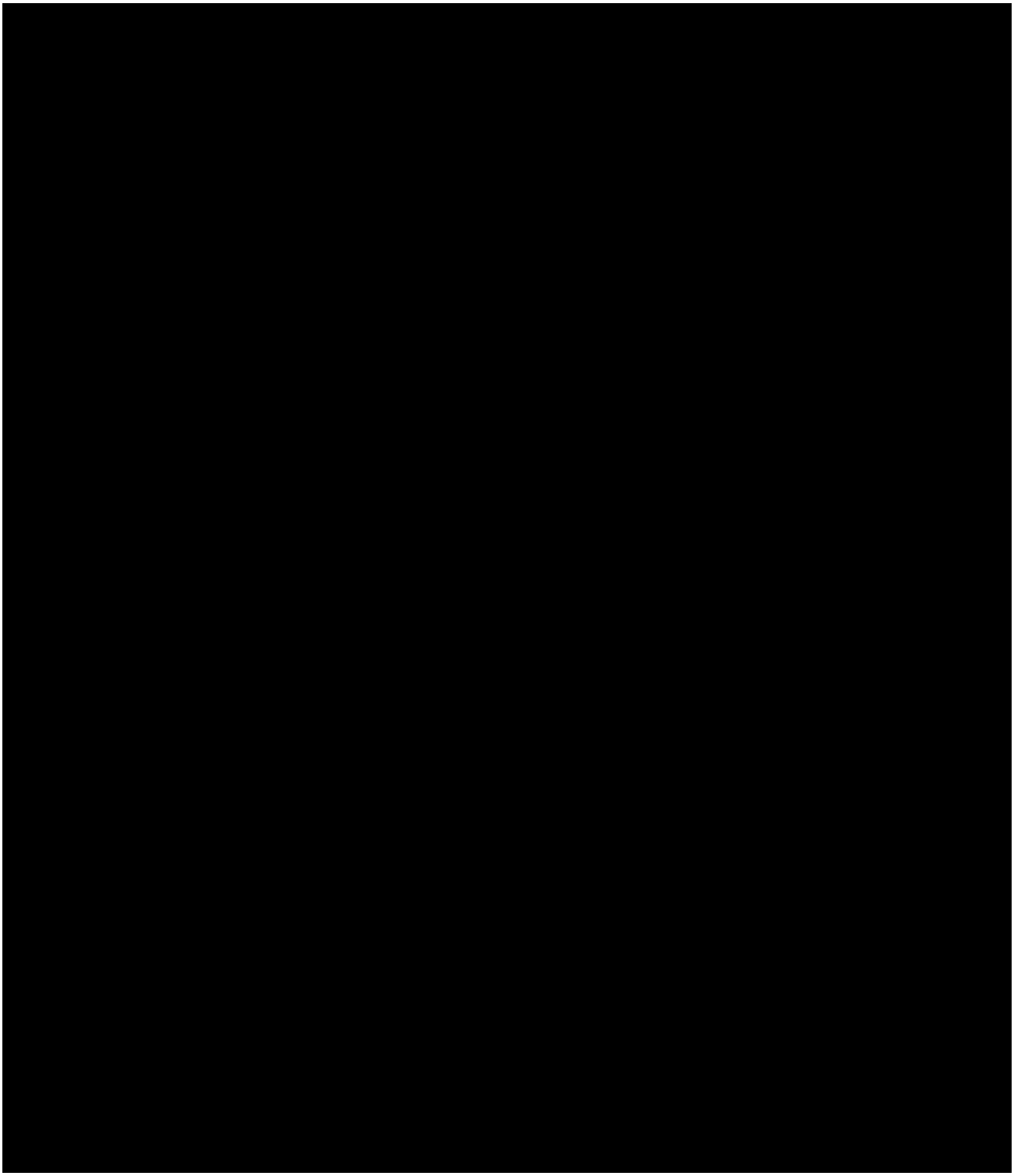


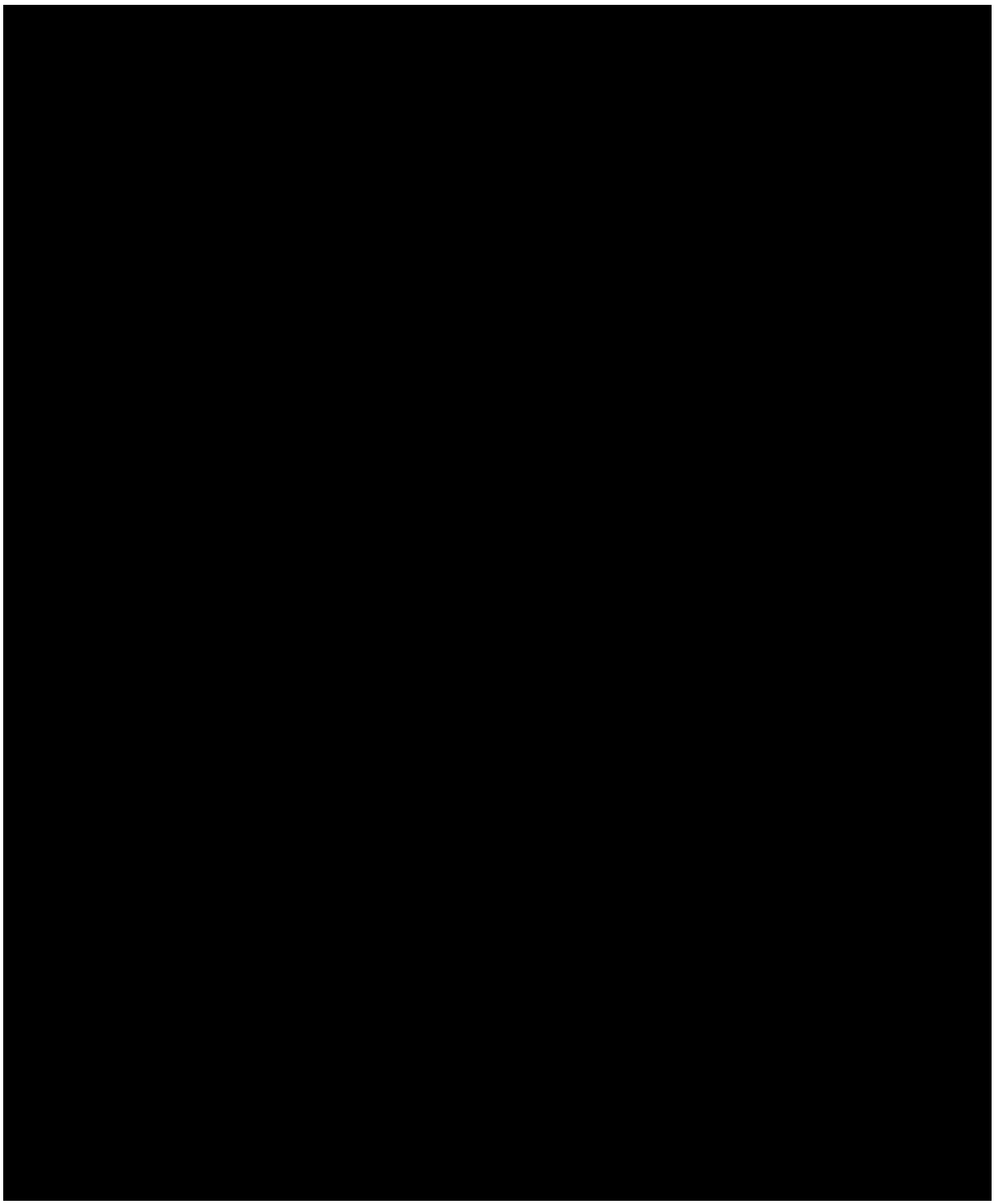


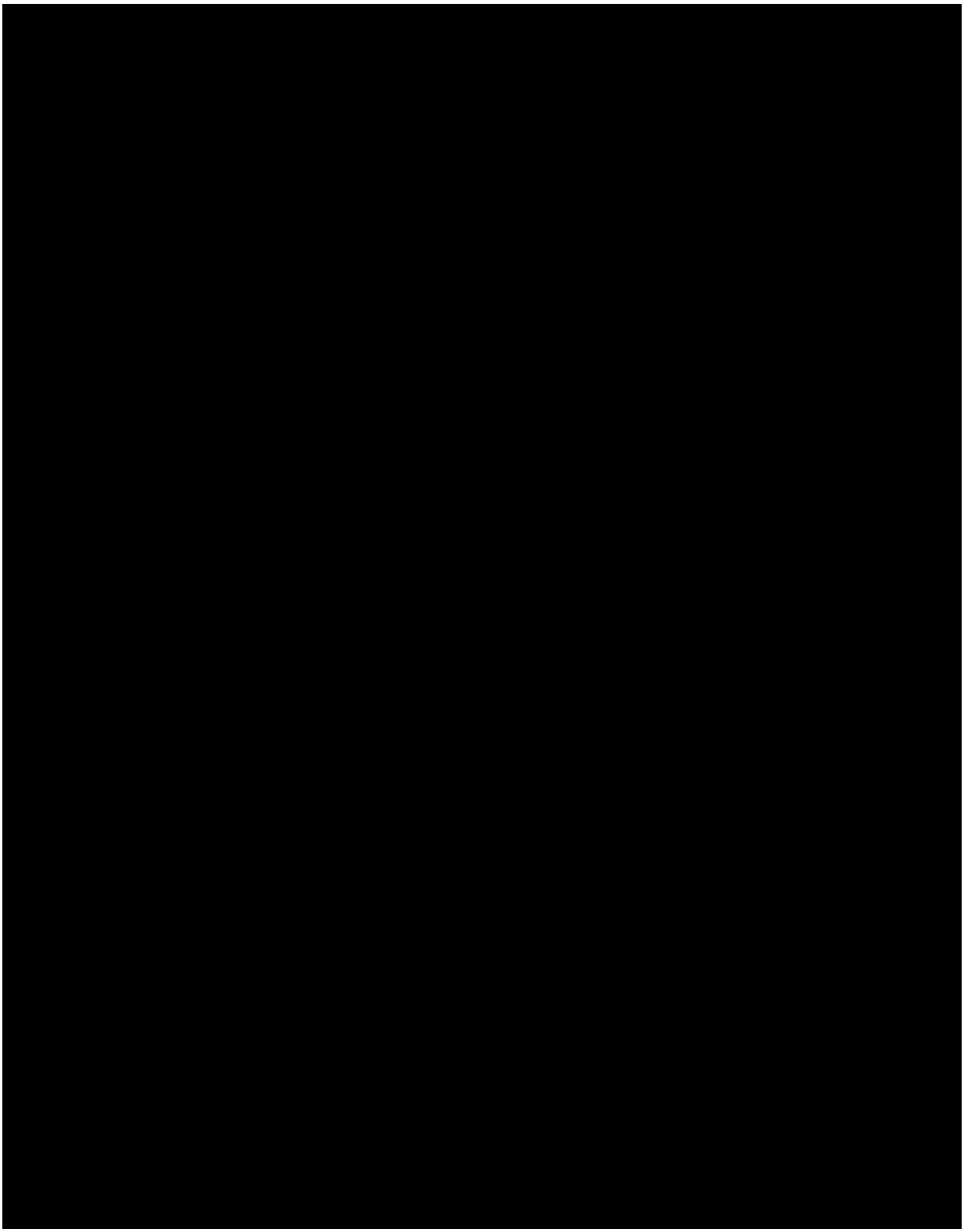


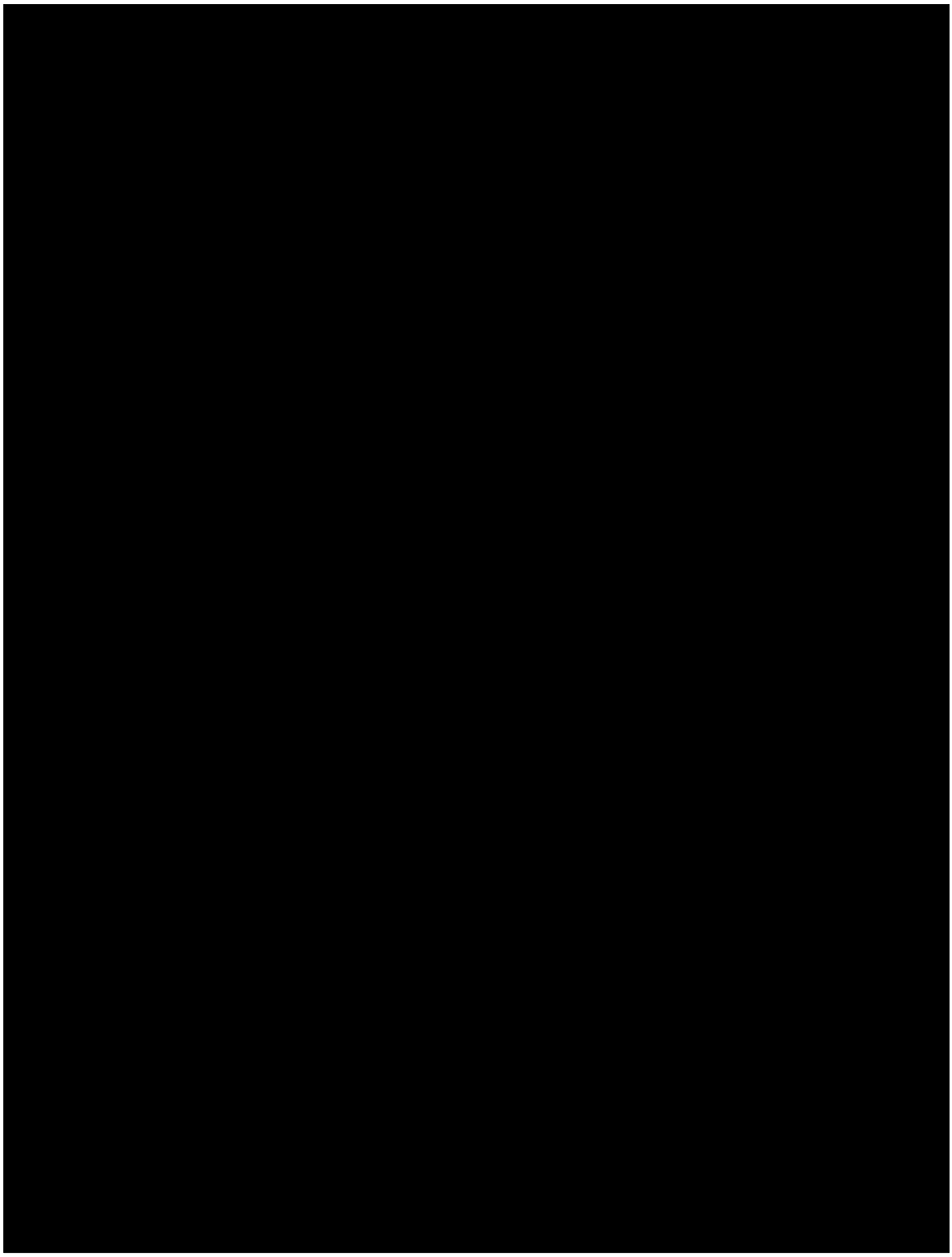


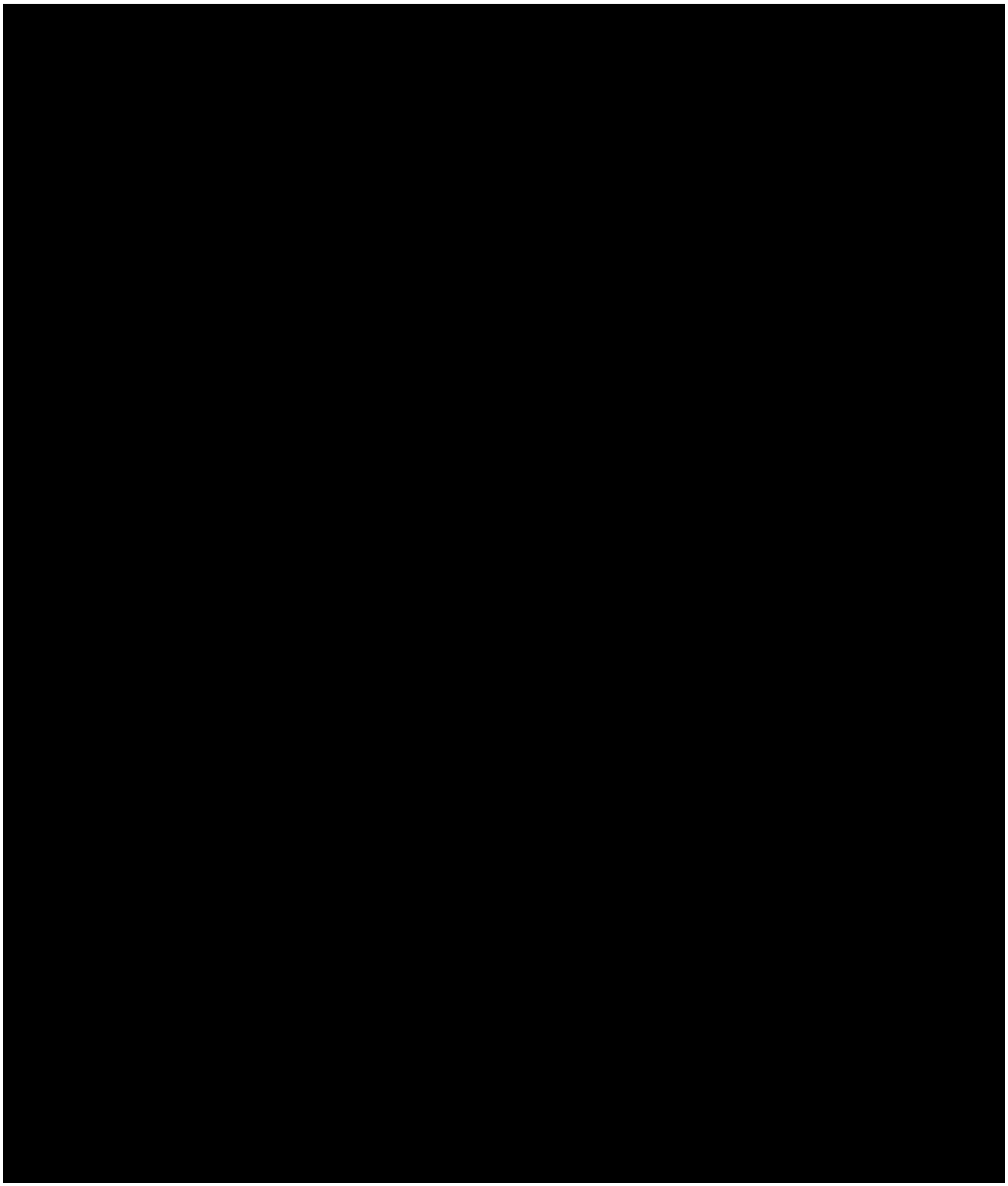


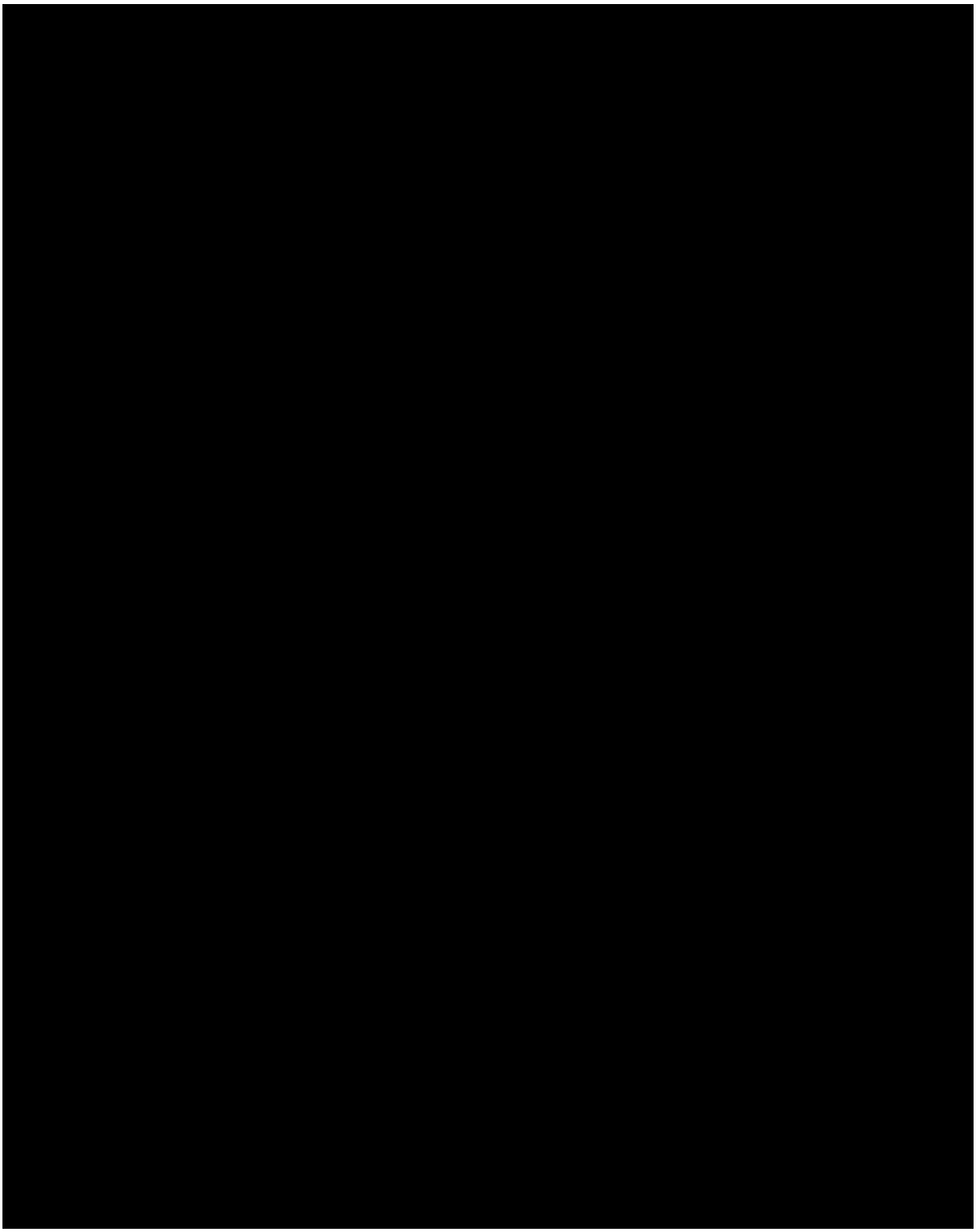


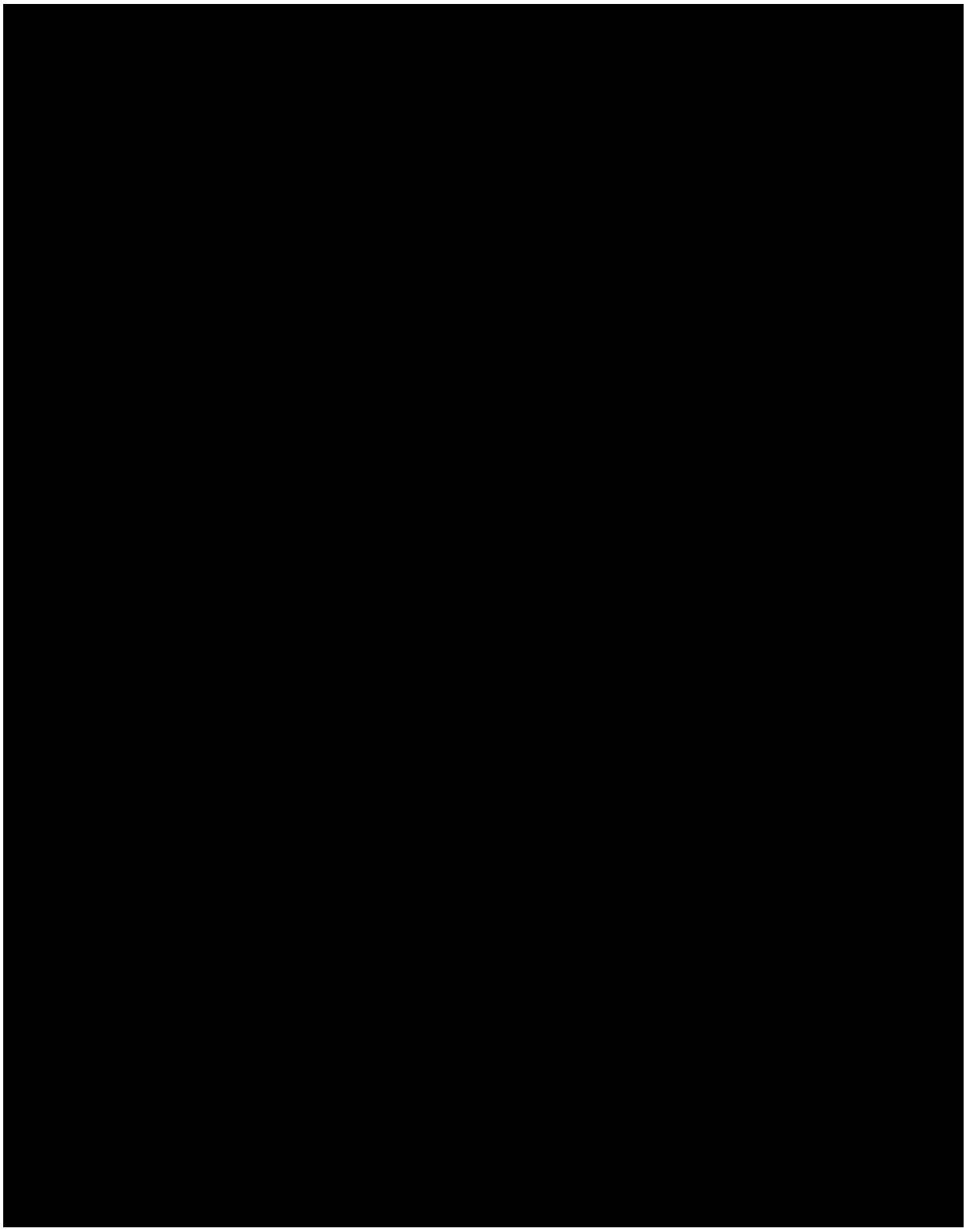


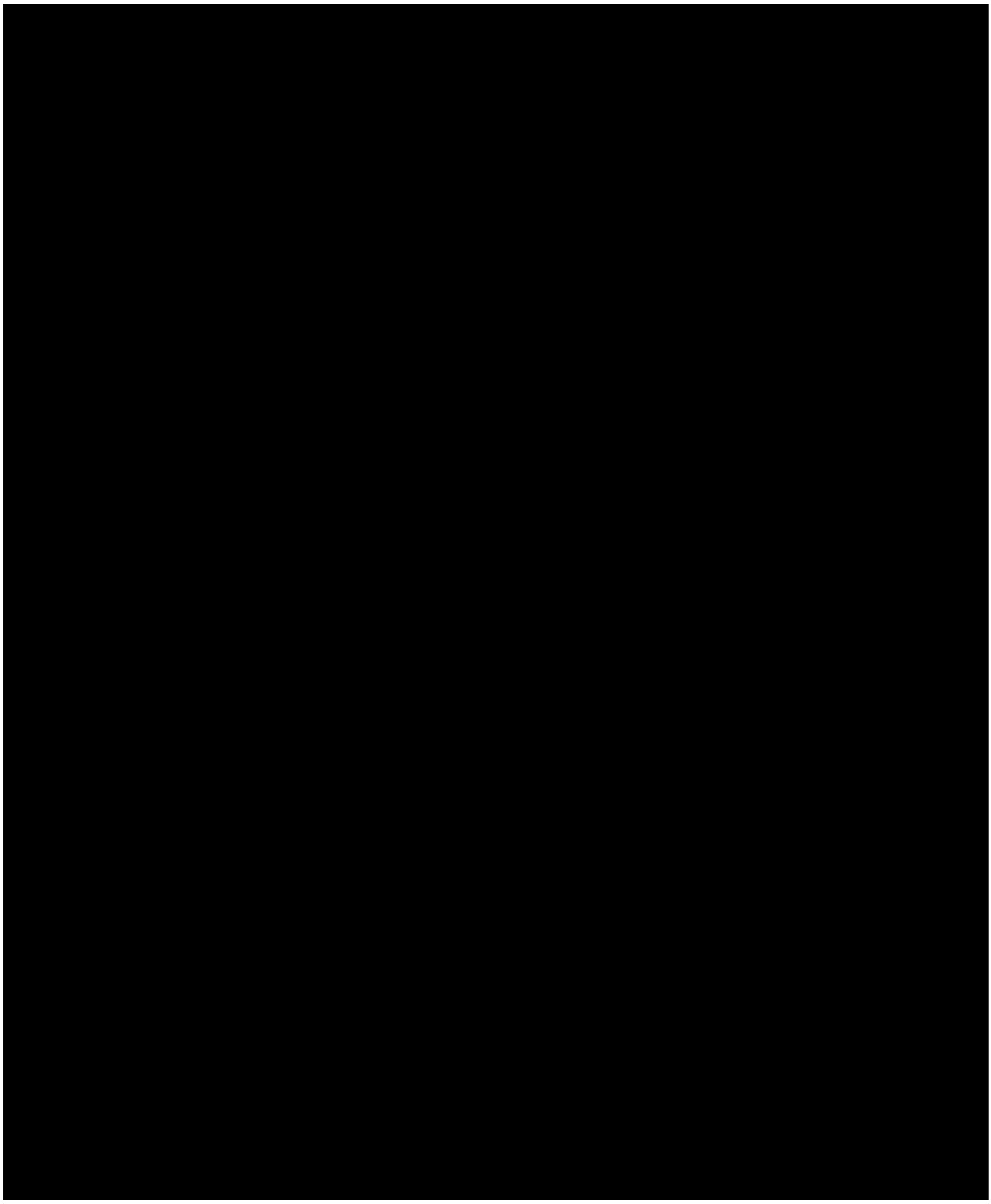


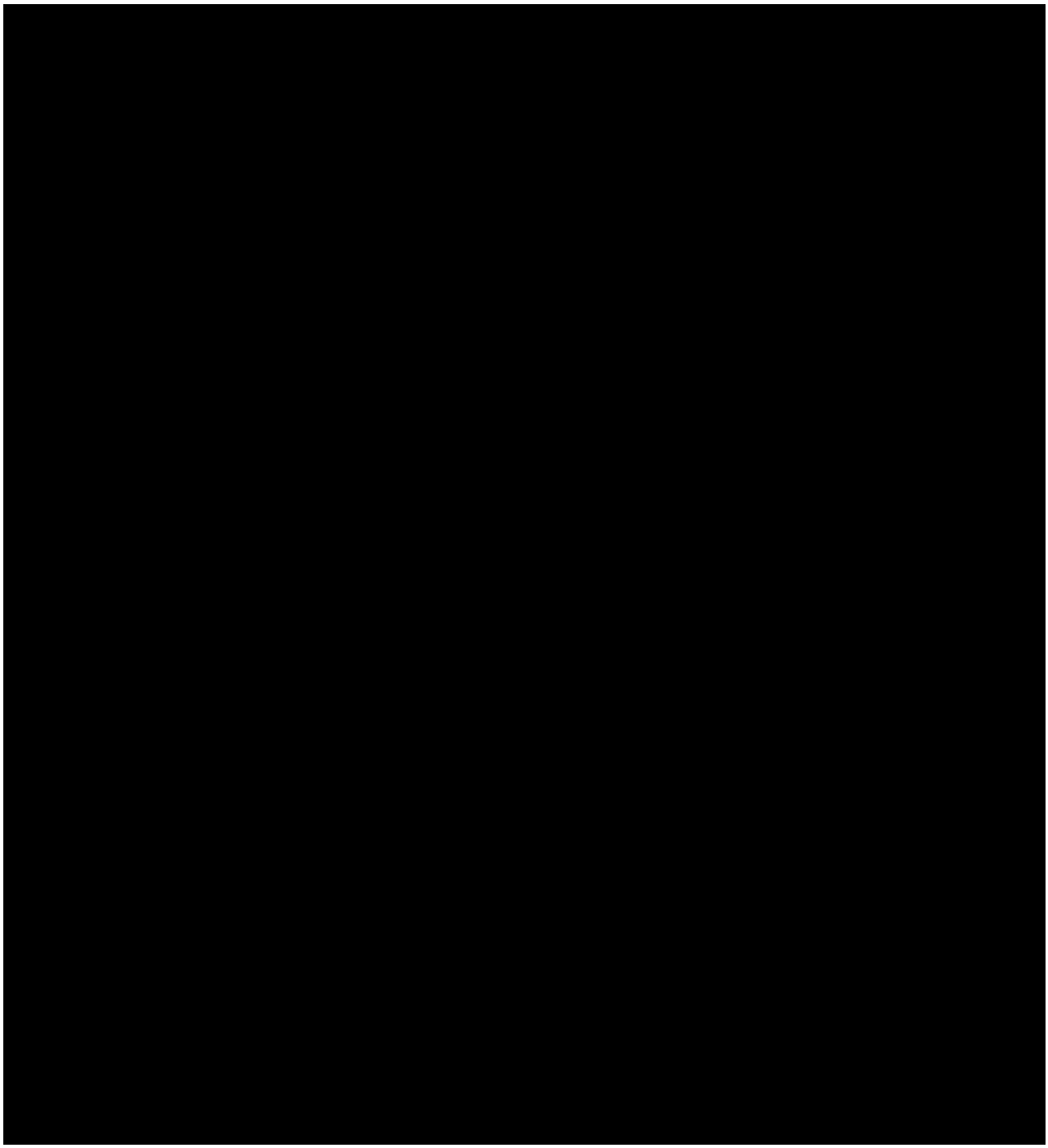


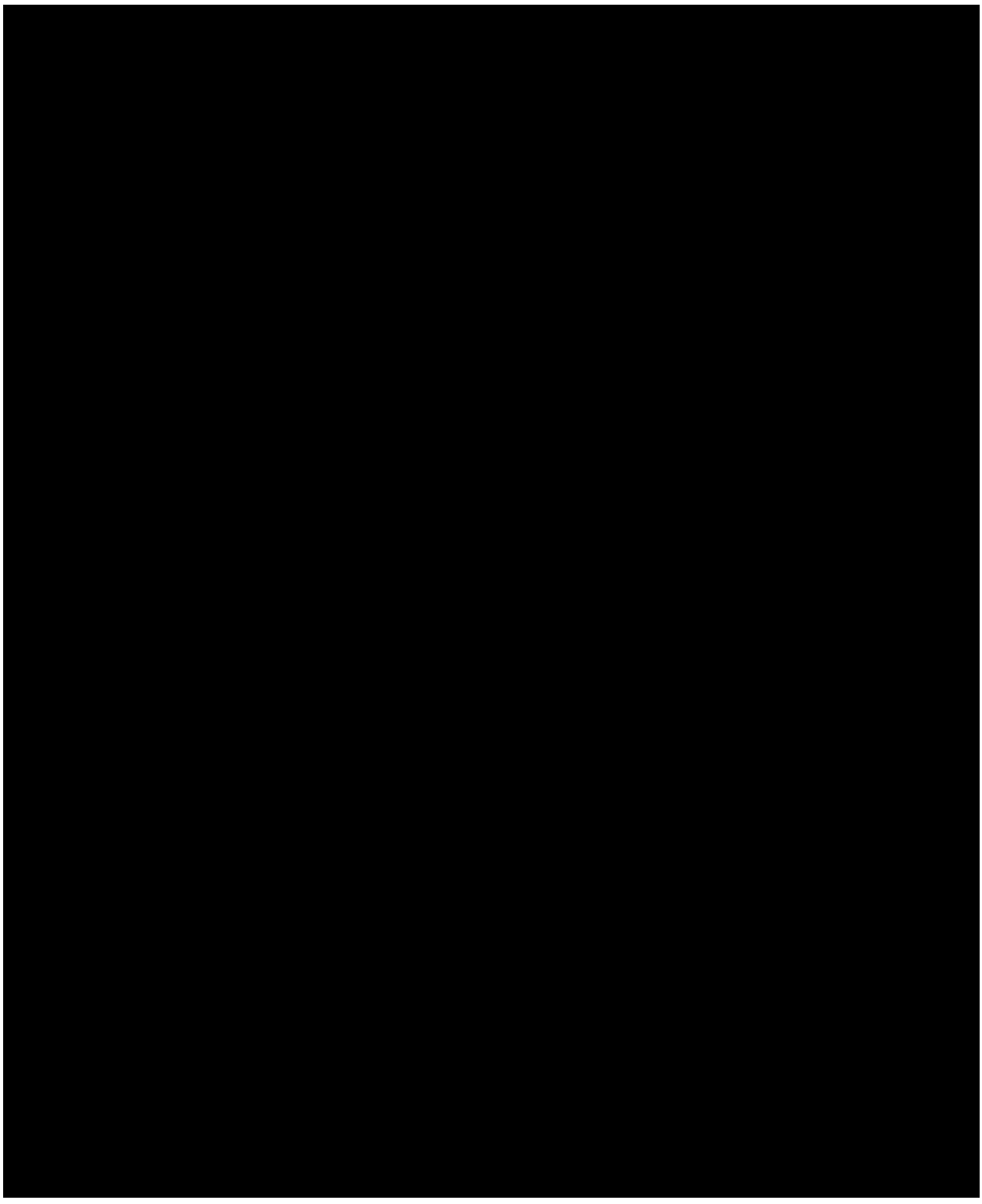


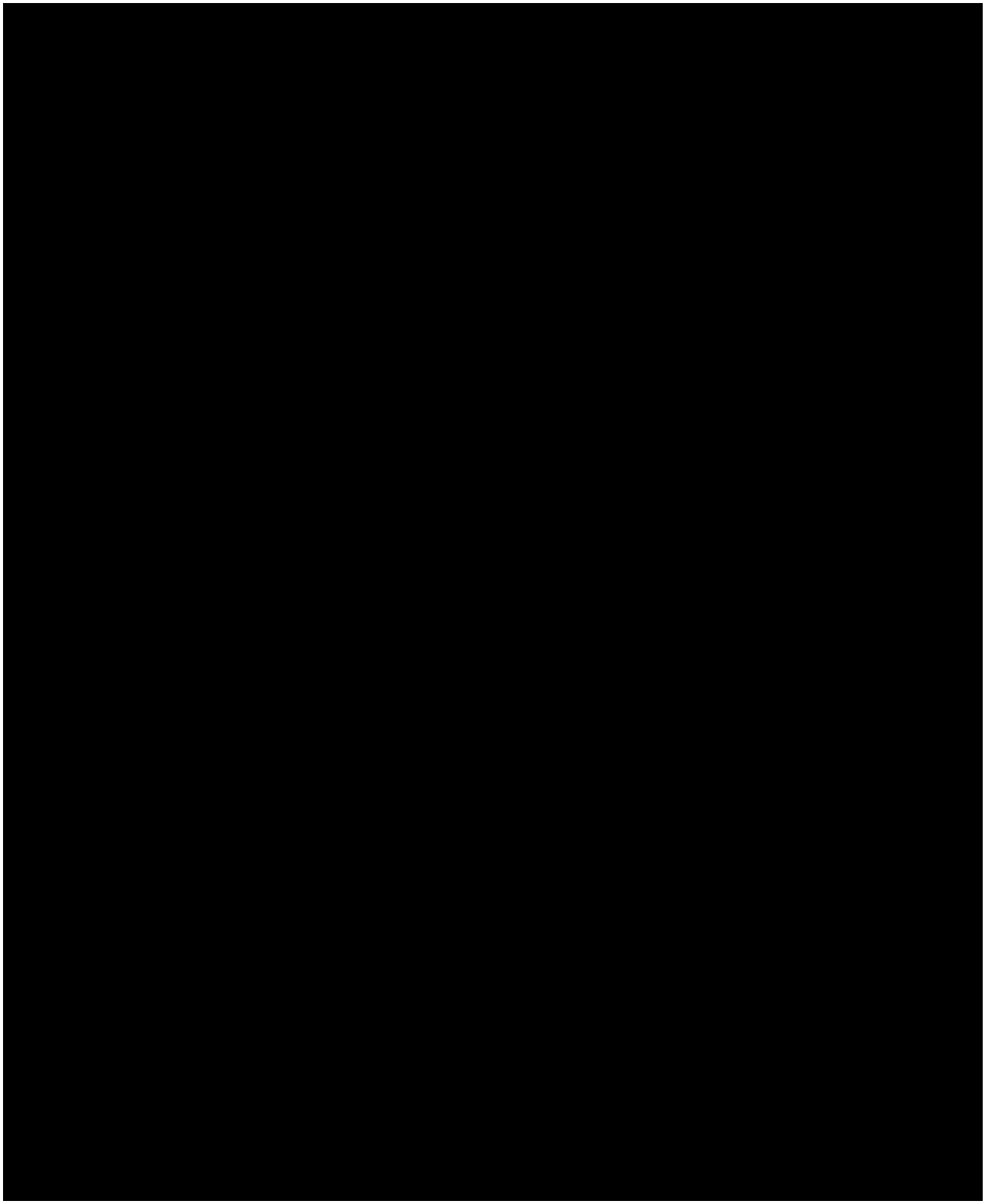


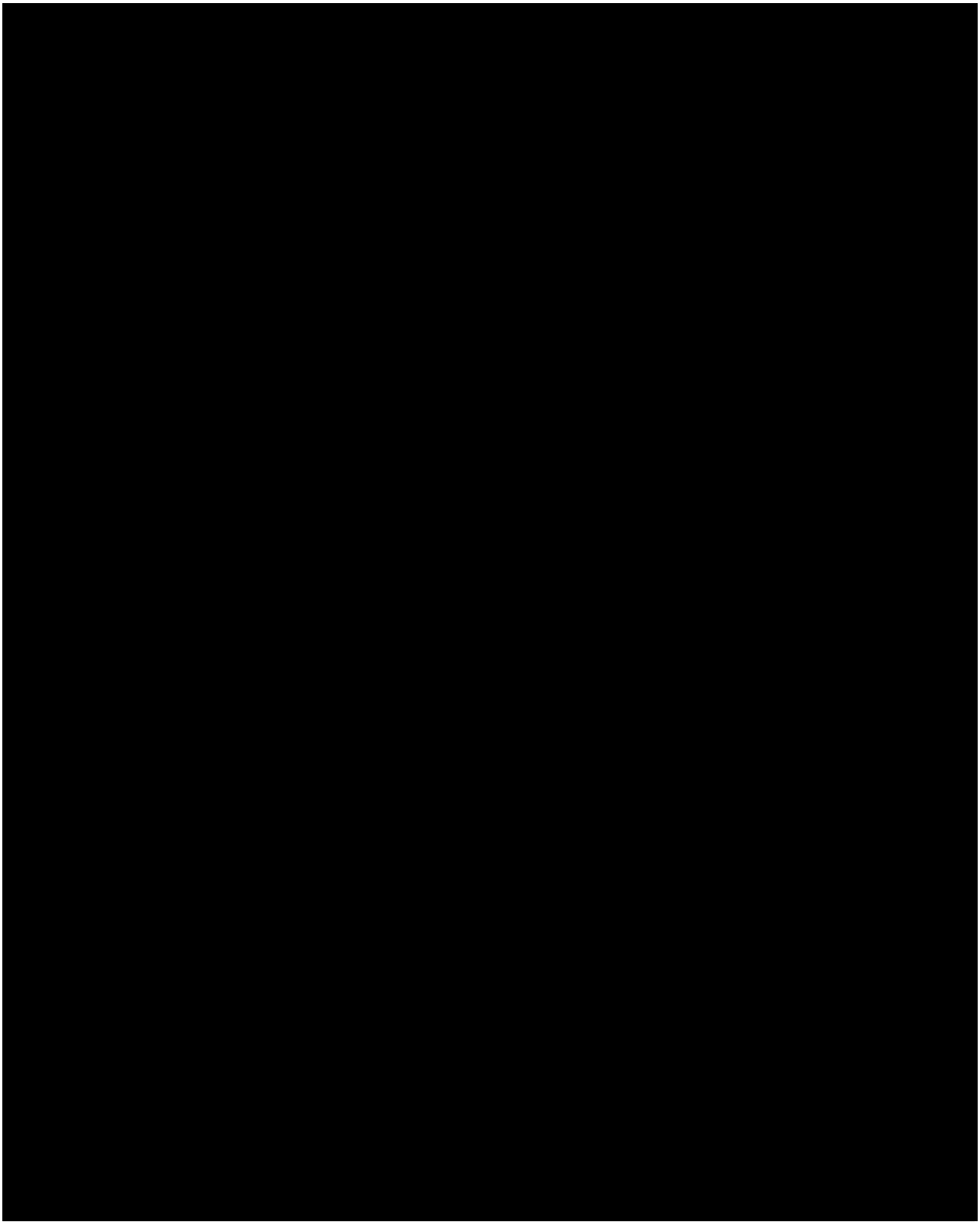


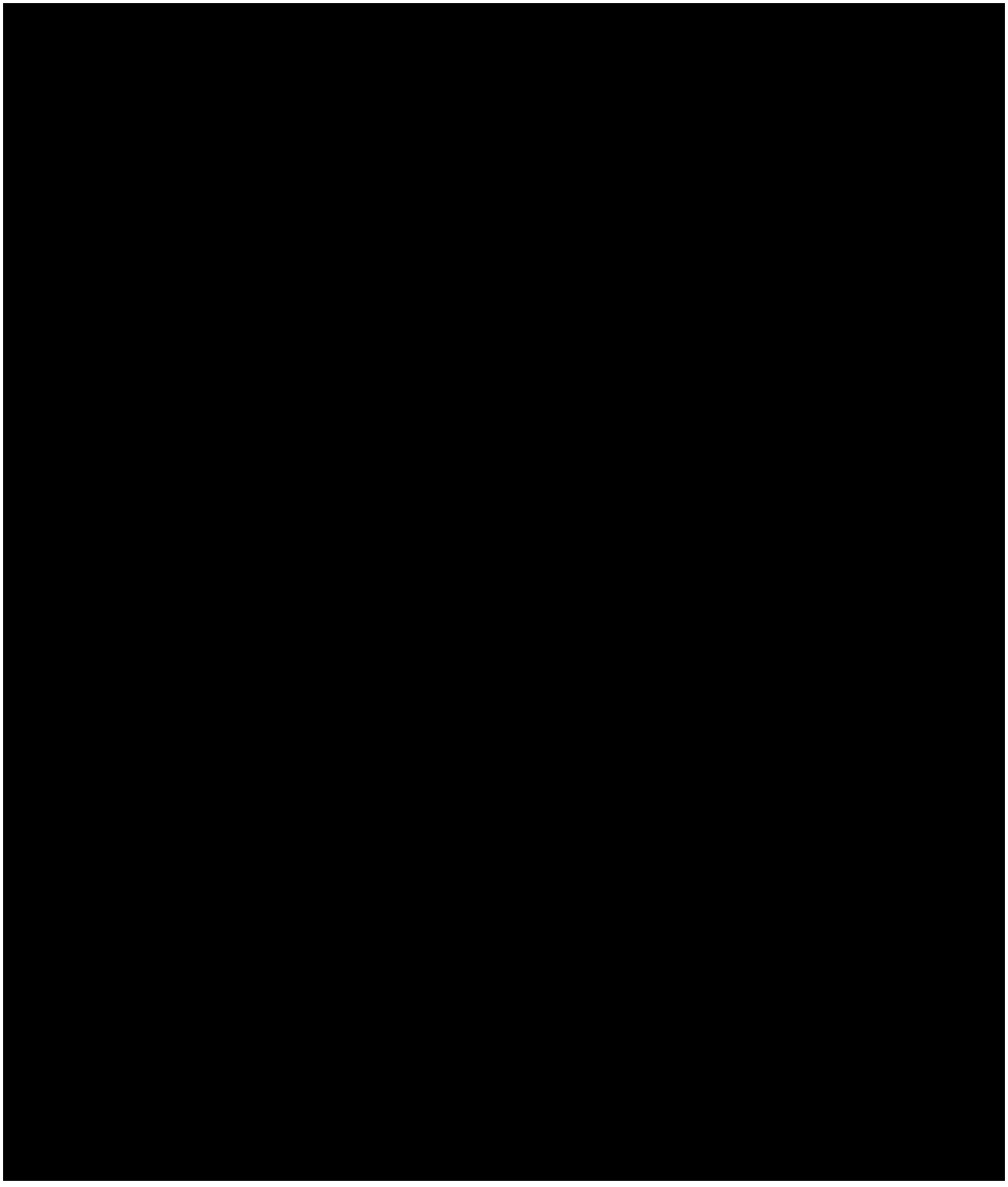


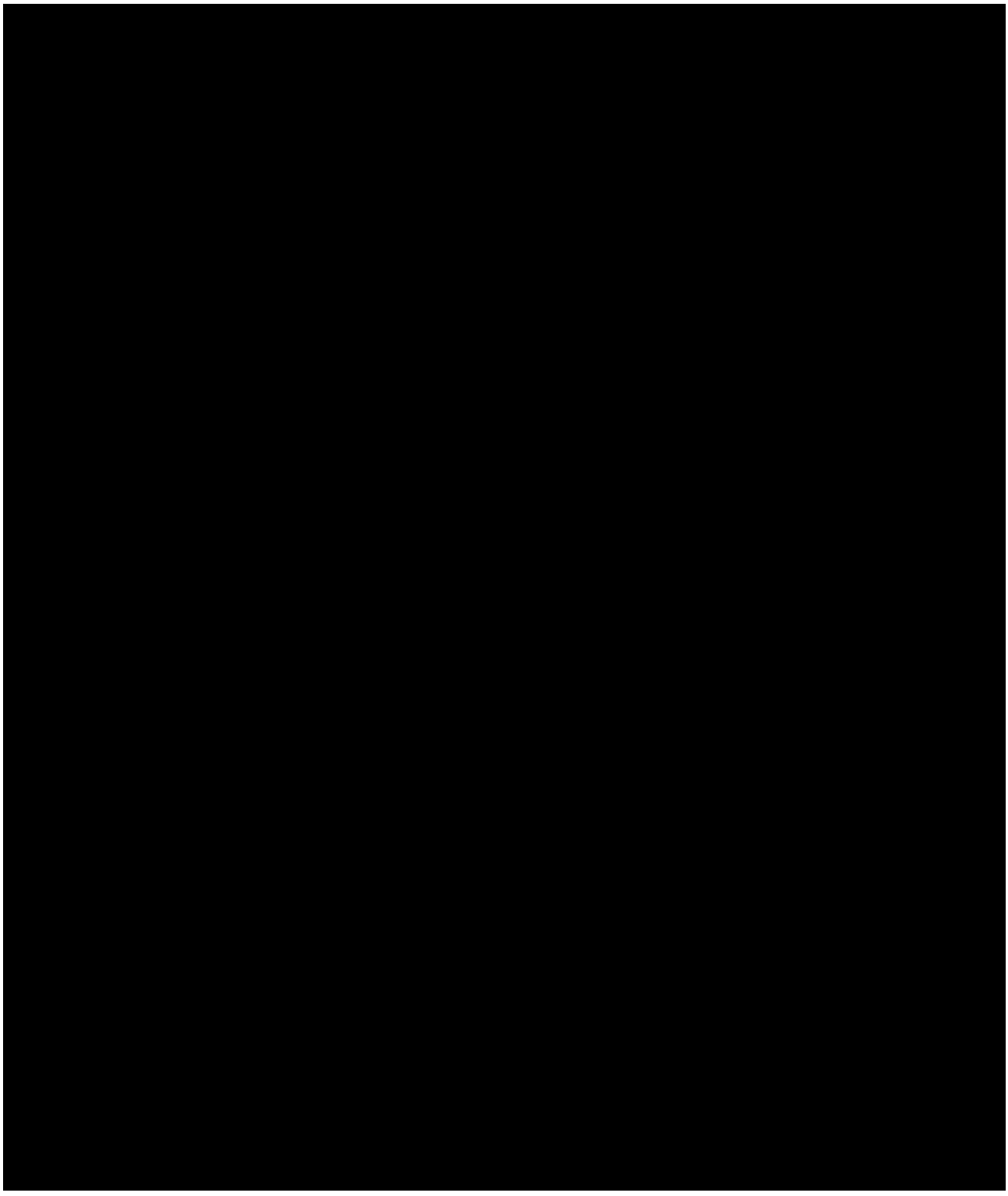


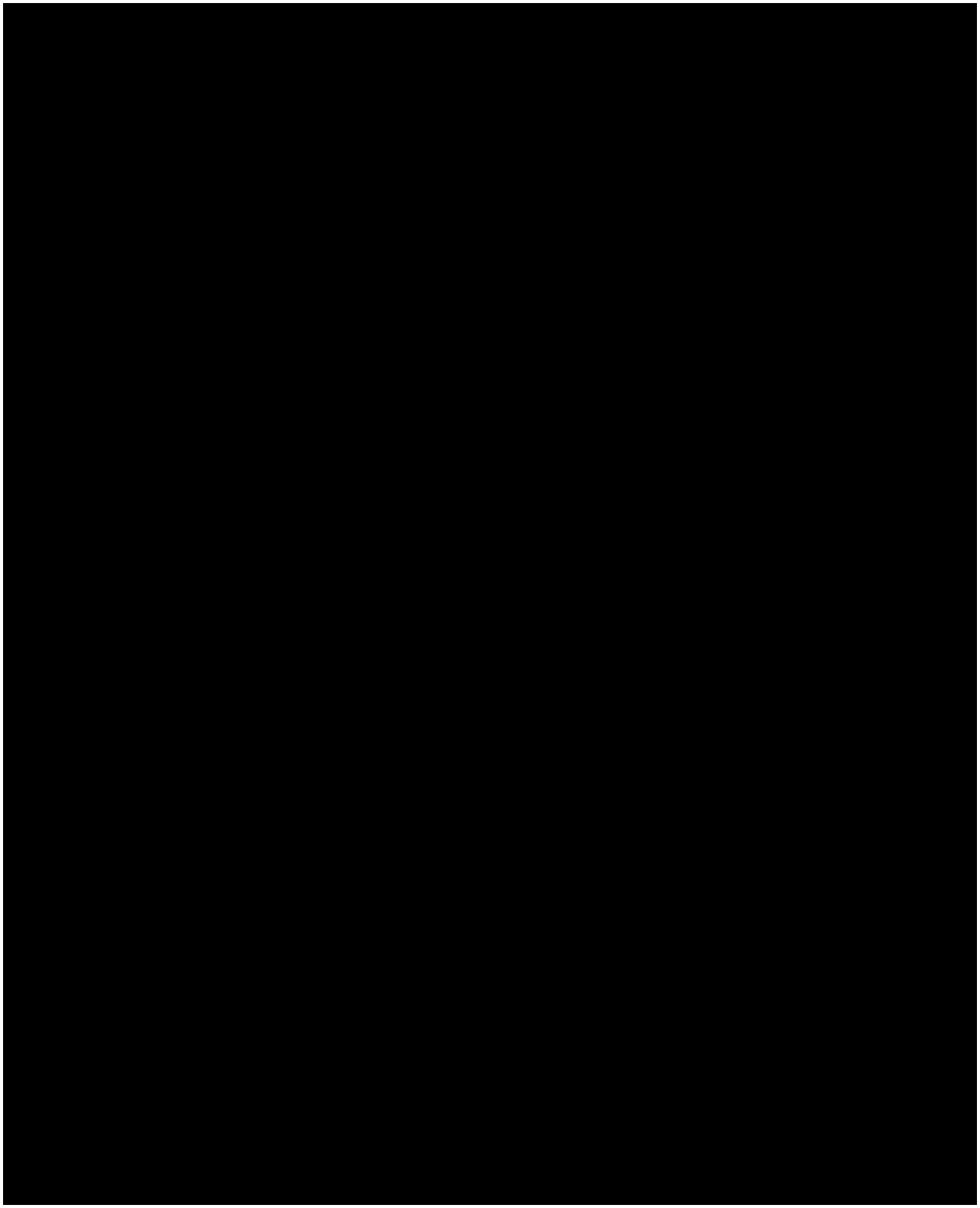












Fwd: Re: WPATH chapter on eunuchs - CONFIDENTIAL

From: [redacted]
To:
Date: Mon, 24 Jan 2022 11:31:12 -0500
Attachments: Eunuchs.doc (29.7 kB)

Dear [redacted]

This is what I sent to [redacted]

[redacted]

[redacted]

-------- Original Message --------

Subject: Re: WPATH chapter on eunuchs
Date: 2022-01-24 15:53
From: [redacted]
To:

Thanks [redacted], I look forward to hearing your views before I open another can of worms.

For completeness I attach my complete review of the Eunuch Chapter.

I struggle with the concept of "Eunuch as a gender identity", but not with the concept of "Eunuch as an identity";

I can understand (I think) "someone who identifies as Eunuch and experiences gender dysphoria (or gender

incongruence), but struggle with the concept of subsuming "Eunuch" as an identity under TGD.

Just very interested to hear your views on this.

Warmest,

[redacted]

[redacted]

On 2022-01-24 15:23, [redacted] wrote:

Hi [redacted] I am out of the area today with very limited internet (have to walk up the hill to get signal). I will reply by tomorrow evening CA time!

Best,

[redacted]

From: [redacted]
Sent: Saturday, January 22, 2022 10:34 AM
To: [redacted]
Subject: Fwd: WPATH chapter on eunuchs

This Message Is From an External Sender
This message came from outside your organization.

Hi [redacted]
Hope you are okay!
I went through entire SOC8: there are some issues with the assessment chapter which I think can be sorted out (with involvement of the entire BOD) and made fit for purpose for the communities WPATH serves.
In addition, there are two very "controversial" (in my view) chapters..... I commented on: Intersex and Eunuch.
I can fully comprehend the concept of people with Intersex and gender dysphoria/gender incongruence and those who identify as Eunuch with gender dysphoria/gender incongruence, but NOT all Eunuchs and people with Intersex indiscriminately..... makes no sense to me!
Anyhow, see response from one of the Working Group Chairs below..... I would really appreciate a chat with you about this before I step this up, because I am not letting this go for the sake of anyone other than following logic and reason,
All in confidence ofcourse,

With warm wishes,

[redacted]

[redacted]

Begin forwarded message:

From: [redacted]
Date: 22 January 2022 at 19:02:07 CET
To: [redacted]
Cc: [redacted]
Subject: WPATH chapter on eunuchs

Dear [redacted]

As the chapter lead for the WPATH Standards of Care chapter on eunuchs, I was very surprised and disappointed by your very long set of comments about the chapter. Yours was one of the longest and the most negative. I was especially struck by two of the comments that you made:

1. There is the creation of a new term "Male-to-Eunuch gender dysphoria", which does not exist in any diagnostic health classification system, or indeed in any scientific literature published in reputable peer-reviewed journals, or medical textbooks.

The term "Male-to-Eunuch was fully described and discussed in two articles in the **International Journal of Transgenderism:**

> Vale K, Johnson TW, Jansen MS, Lawson BK, Lieberman T, Willett KH, Wassersug RJ. (2010). The development of standards of care for individuals with a male-to-eunuch gender identity disorder. *International Journal of Transgenderism*; 12:40-51.
>
> Johnson TW, Wassersug RJ. (2016). Recognition of gender variants outside the binary in WPATH Standards of Care, Version 7.0. *International Journal of Transgenderism*; 17:1-3.

There are also articles in a number of other peer-reviewed journals, including the Archives of Sexual Behavior, the Journal of Sexual Medicine, and Asian Journal of Andrology. Articles discussing Male-to-Eunuch have been cited in over 100 articles published in a wide variety of journals and book chapters.

You also wrote:

1. I have been working full-time as a trans health specialist providing psychological support, endocrine treatment (initiation, dosing, and monitoring of gender affirming hormone treatment), and referral for gender affirming surgeries for my patients since 2007. I have treated thousands of TGD people with gender affirming hormone treatment. Our Centre has approximately 3000 current patients and we receive in excess of thousand new referrals per annum. I have NEVER met a patient who identified as Eunuch and consequently, I am extremely sceptical about the veracity of this Chapter.

I have been conducting research on the eunuch community for nearly 20 years and my name is known within the community. As a result, I have had a number of individuals seeking professional care contact me to see if I might help them to find counselors or medical practitioners to help them to obtain surgical castration and/or appropriate hormone treatment.

Several years ago, before I knew better, I referred two individuals seeking care to the Nottingham Centre for Transgender Health. Both reported back to me that felt that their treatment was dismissive and abusive. I have referred no one further to the Centre. Male-to-Eunuch individuals have been there but have not been recognized. This is why the chapter on eunuchs is so important to have in the new Standards of Care. Eunuchs exist, and they require recognition and proper treatment.

I hope that you will reconsider your comments on our chapter.

Sincerely,

[redacted]

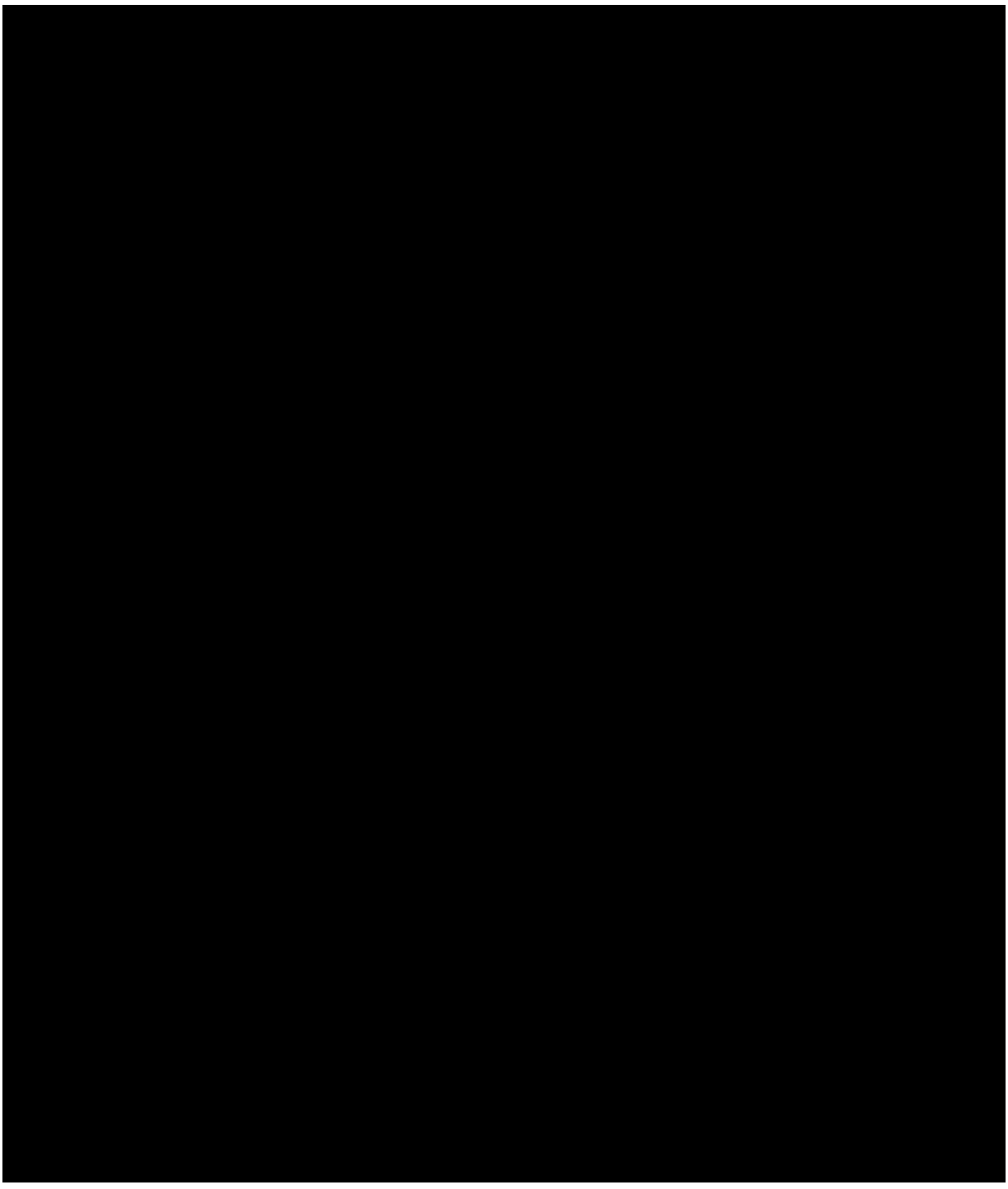
This Chapter is entitled "Eunuch"

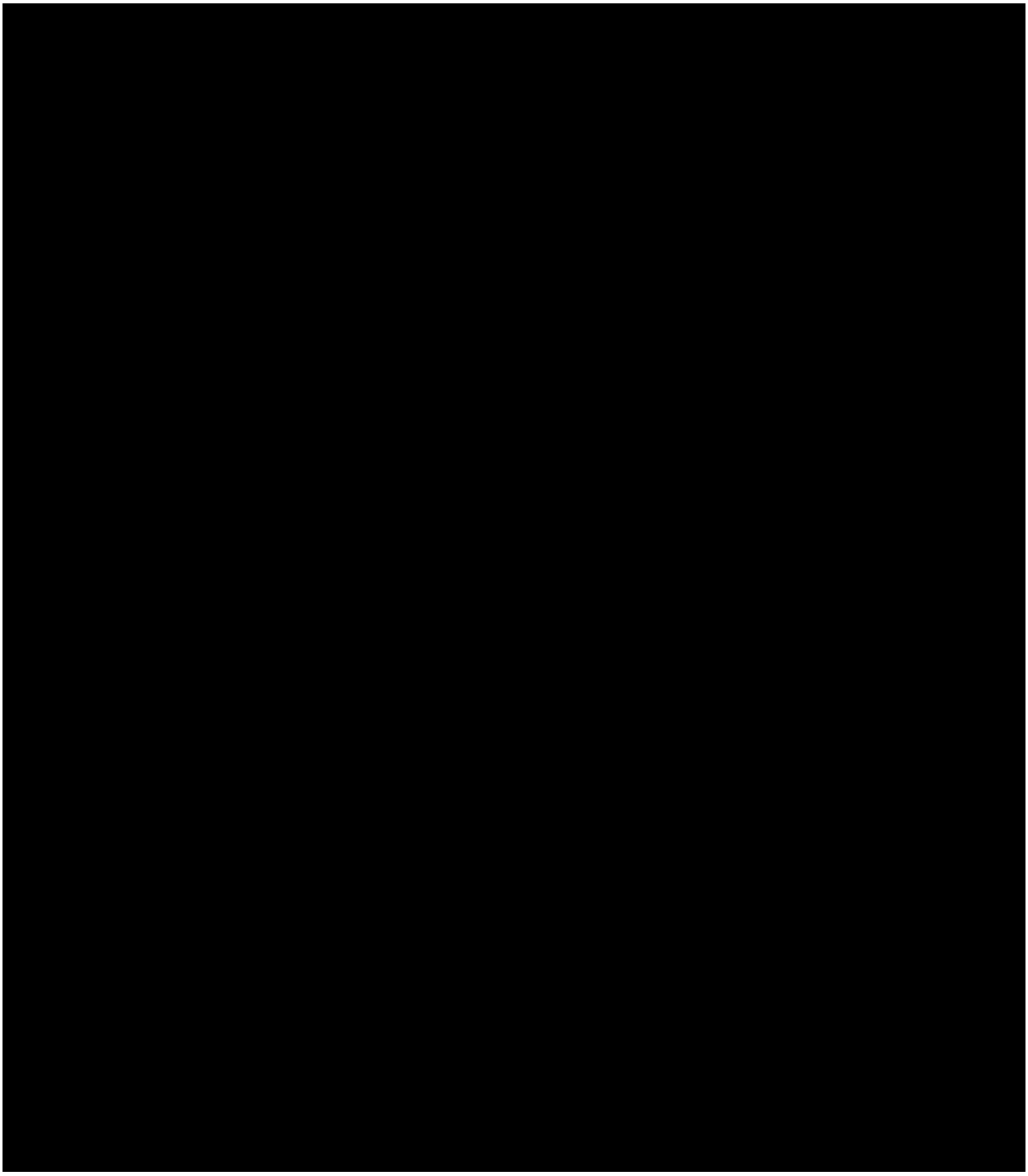
The definition of an eunuch is a man who has been castrated.

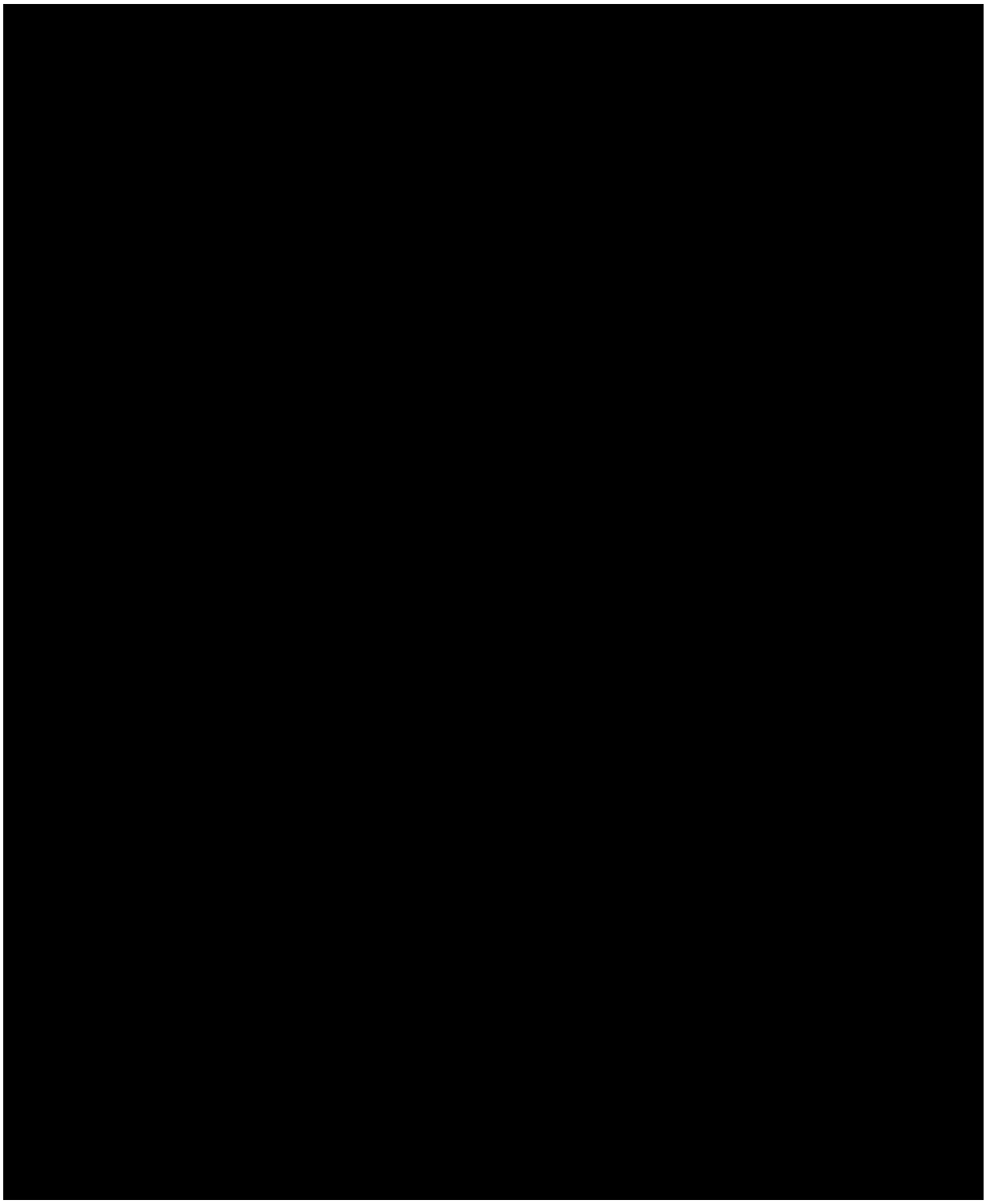
I have very serious misgivings about this entire Chapter for a number of reasons:

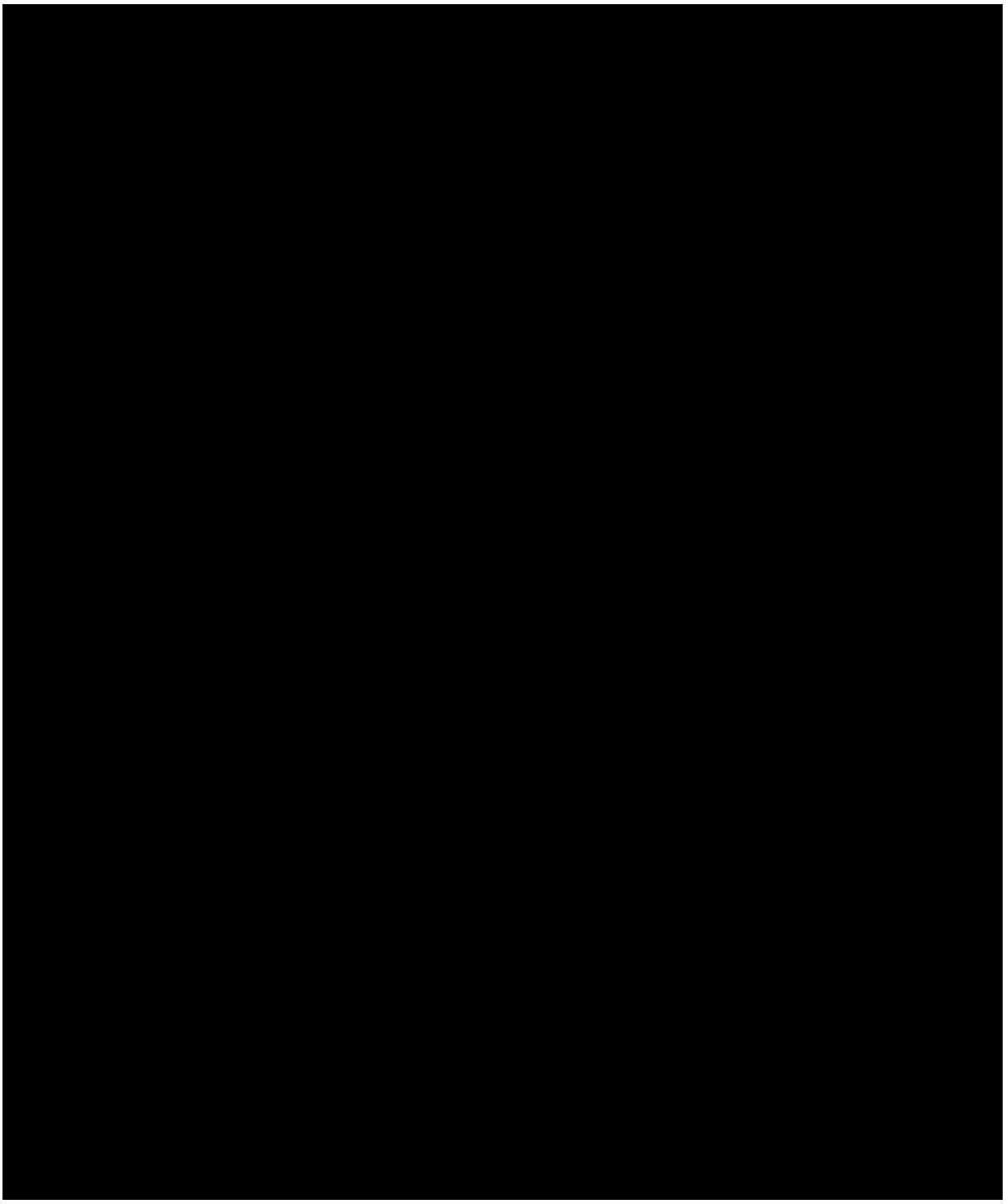
1. **The Chapter makes a number of claims, such as "many people who benefit from gender affirming medical care, those who identify as eunuch are the least visible", "eunuch-identified individuals are in need of gender affirming services", "the identity of eunuch is a gender identity of its own", etcetera etcetera, and the only evidence to underpin these claims is 1 website "the Eunuch Archive" established in 1998 and a repeated claim that "Eunuch-identified people usually are less visible than other gender minorities (Wassersug & Lieberman, 2010)" [read: invisible].**
2. **Eunuch as an identity is not recognized by any reputable global health organization, such as the WHO.**
3. **Eunuch is not classified as a bona fide condition in the ICD-11 (WHO, 2019), or indeed in the DSM-5 (APA, 2013), or any other diagnostic health classification system.**
4. **There is significant historical and cultural misappropriation of the term Eunuch within this Chapter.**
5. **This Chapter is very high on speculation and assumptions, whilst a robust evidence base is largely absent.**
6. **There are comparisons with and assumptions about TGD people which I do not find appropriate (e.g., It is possible that some non-binary individuals may also seek castration to better align their bodies with their gender without identifying as eunuchs; this group also likely contains eunuch-identified individuals who were seeking a way to obtain the care they needed.).**
7. **There is the creation of a new term "Male-to-Eunuch gender dysphoria", which does not exist in any diagnostic health classification system, or indeed in any scientific literature published in reputable peer-reviewed journals, or medical textbooks.**
8. **The majority of published reference works in this Chapter stems from one single person, who – as far as I am aware is not a HP. I find this concerning.**
9. **I have been working full-time as a trans health specialist providing psychological support, endocrine treatment (initiation, dosing, and monitoring of gender affirming hormone treatment), and referral for gender affirming surgeries for my patients since 2007. I have treated thousands of TGD people with gender affirming hormone treatment. Our Centre has approximately 3000 current patients and we receive in excess of thousand new referrals per annum. I have NEVER met a patient who identified as Eunuch and consequently, I am extremely sceptical about the veracity of this Chapter.**

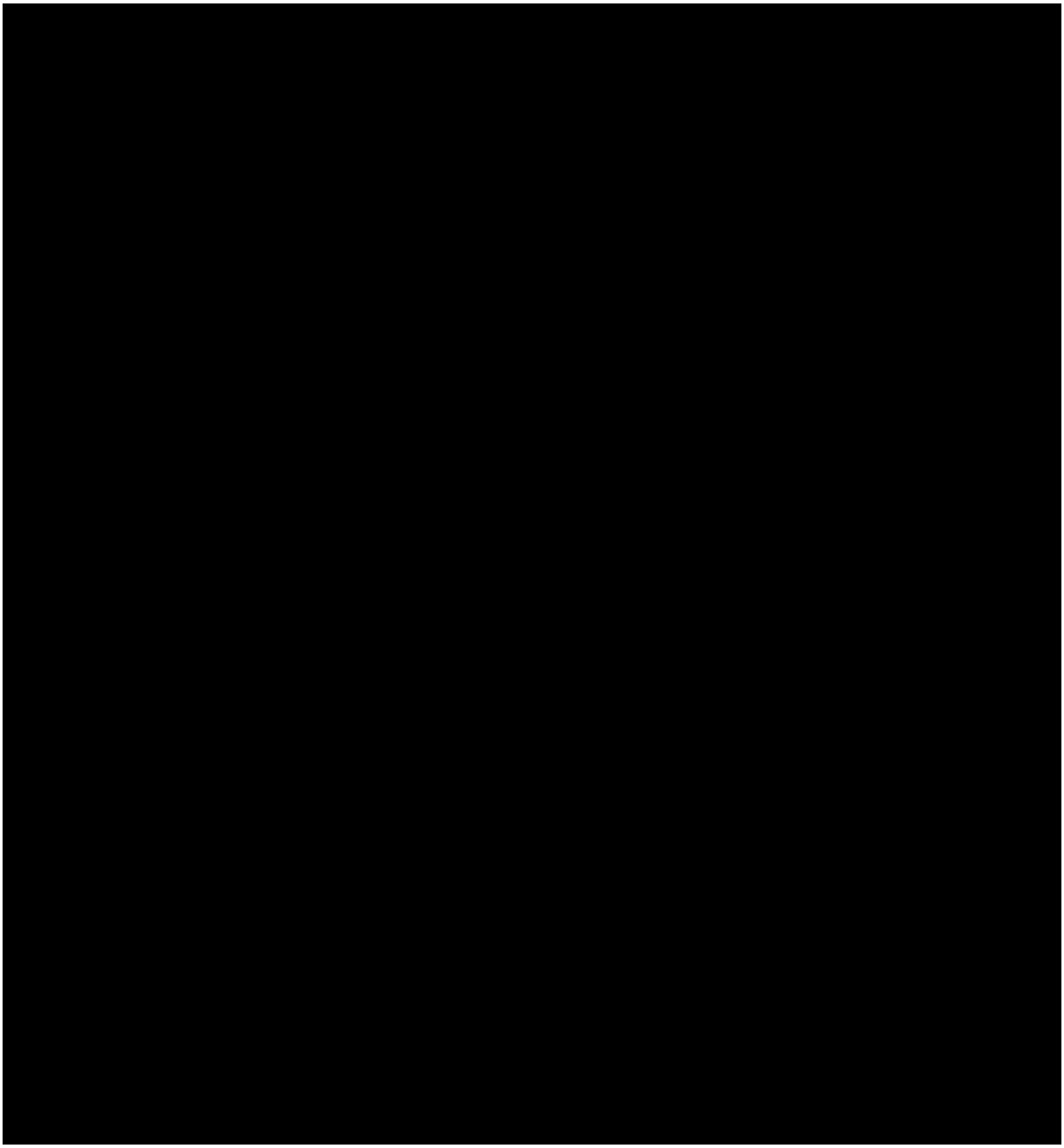
10. Regarding the use of references (in the text and in the references section): please use APA-7 style as is the IJTH referencing housestyle.











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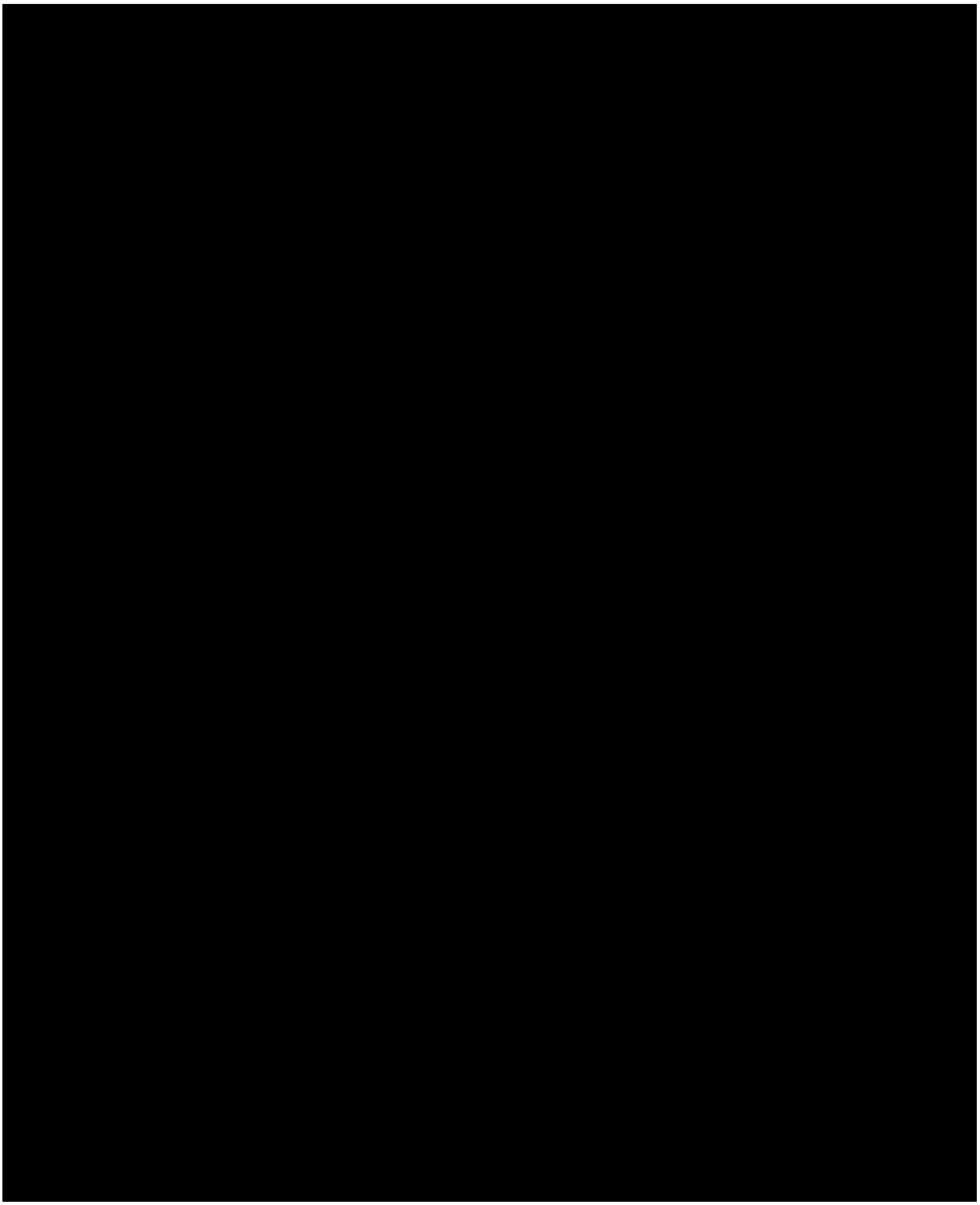

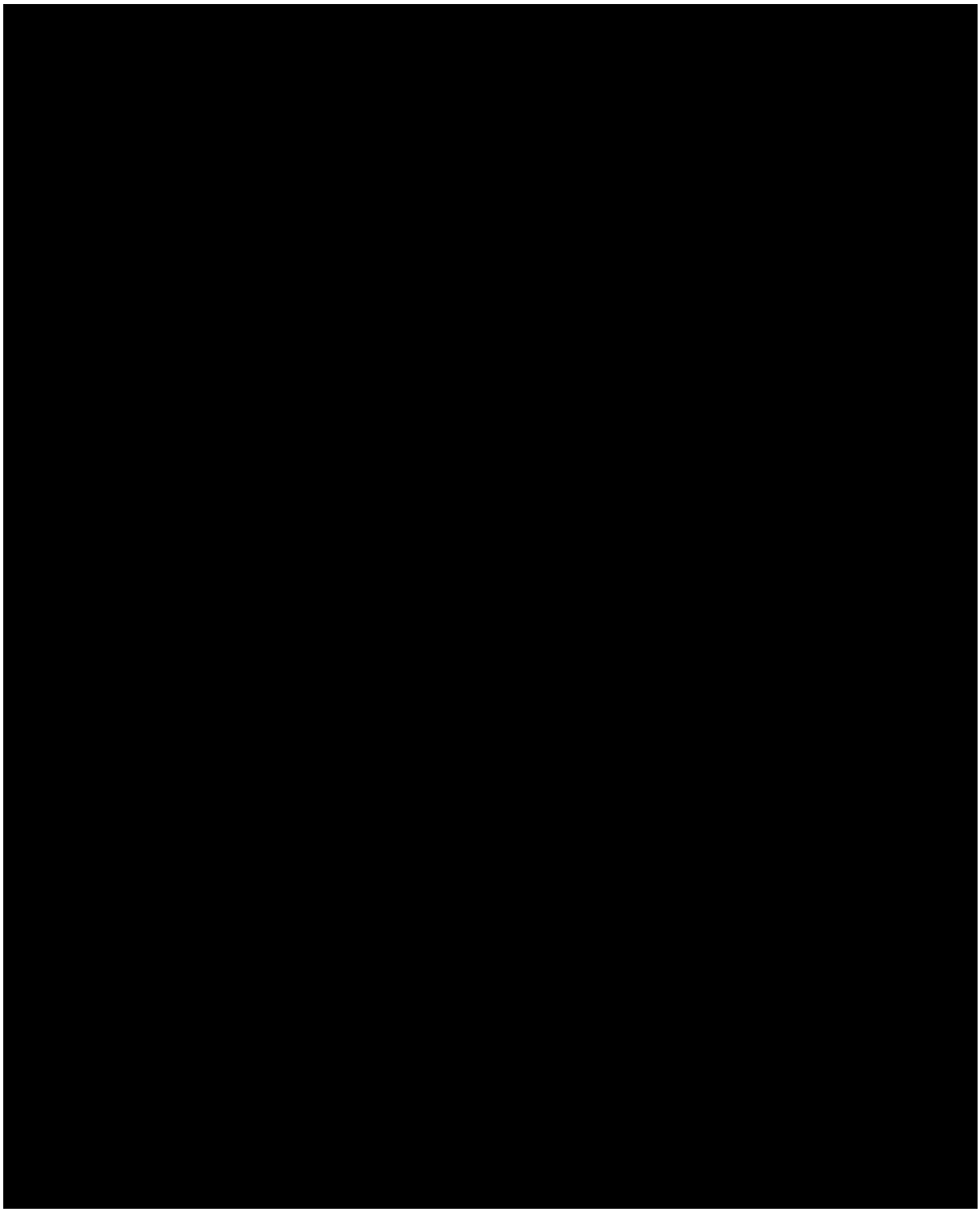

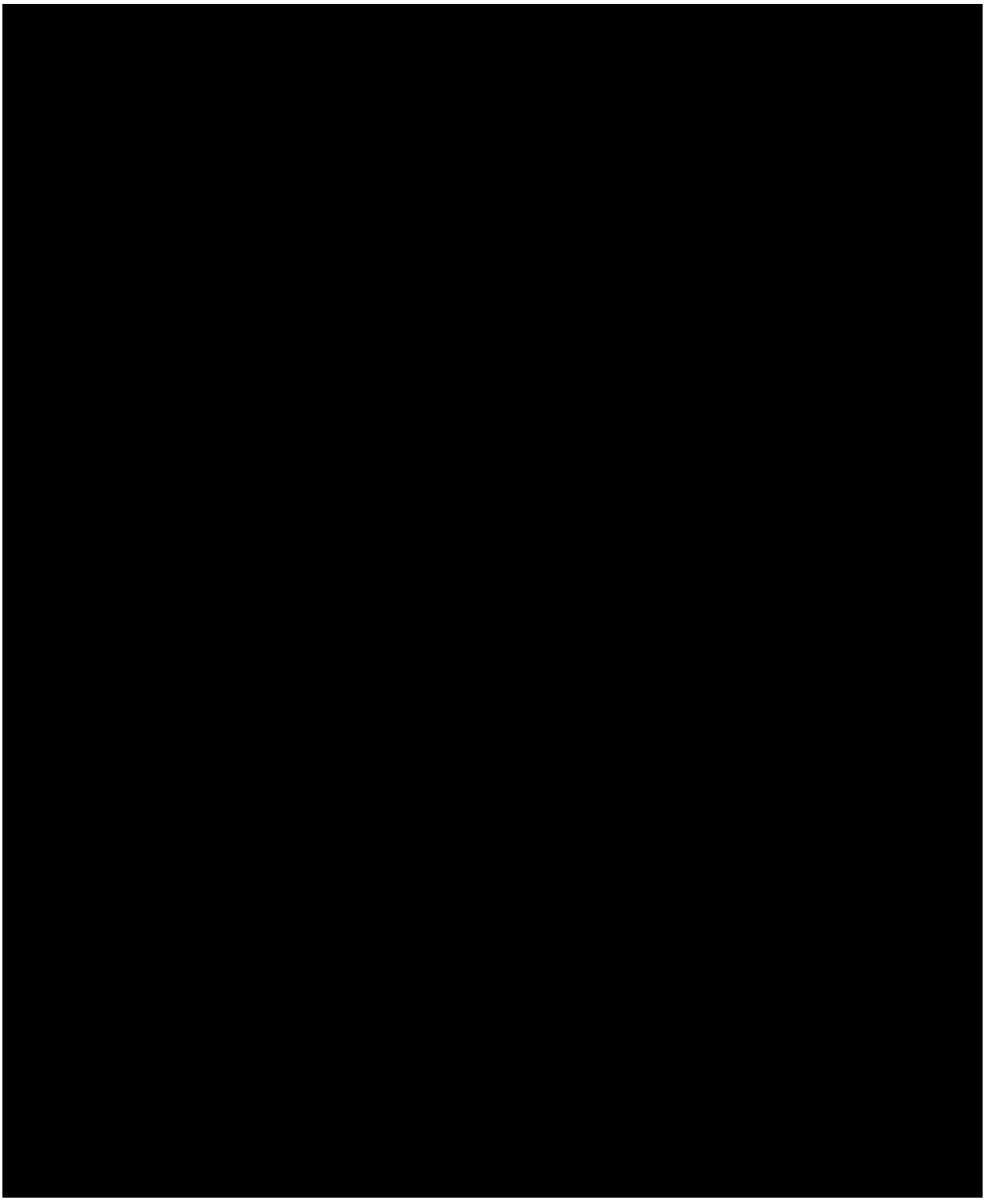

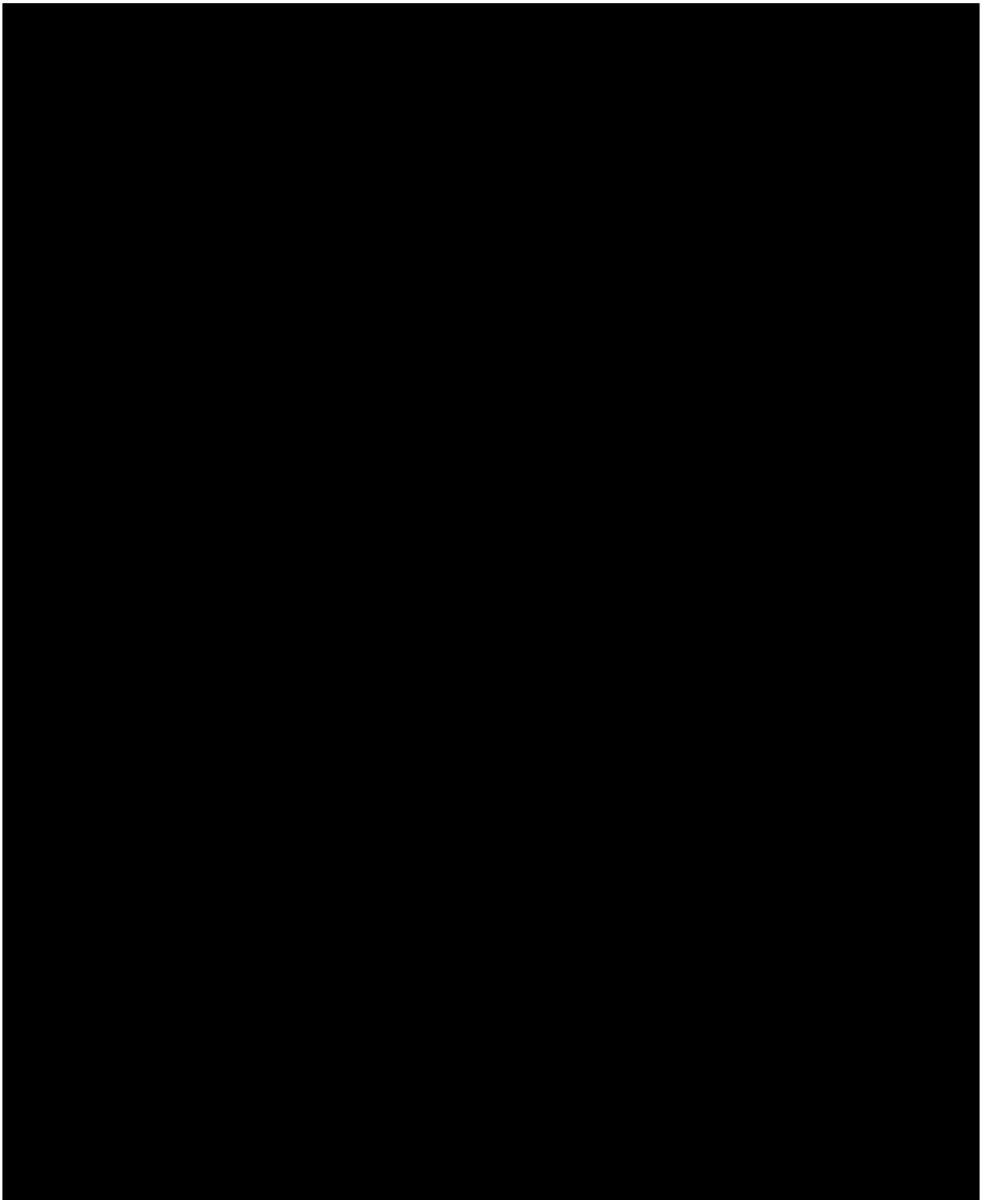

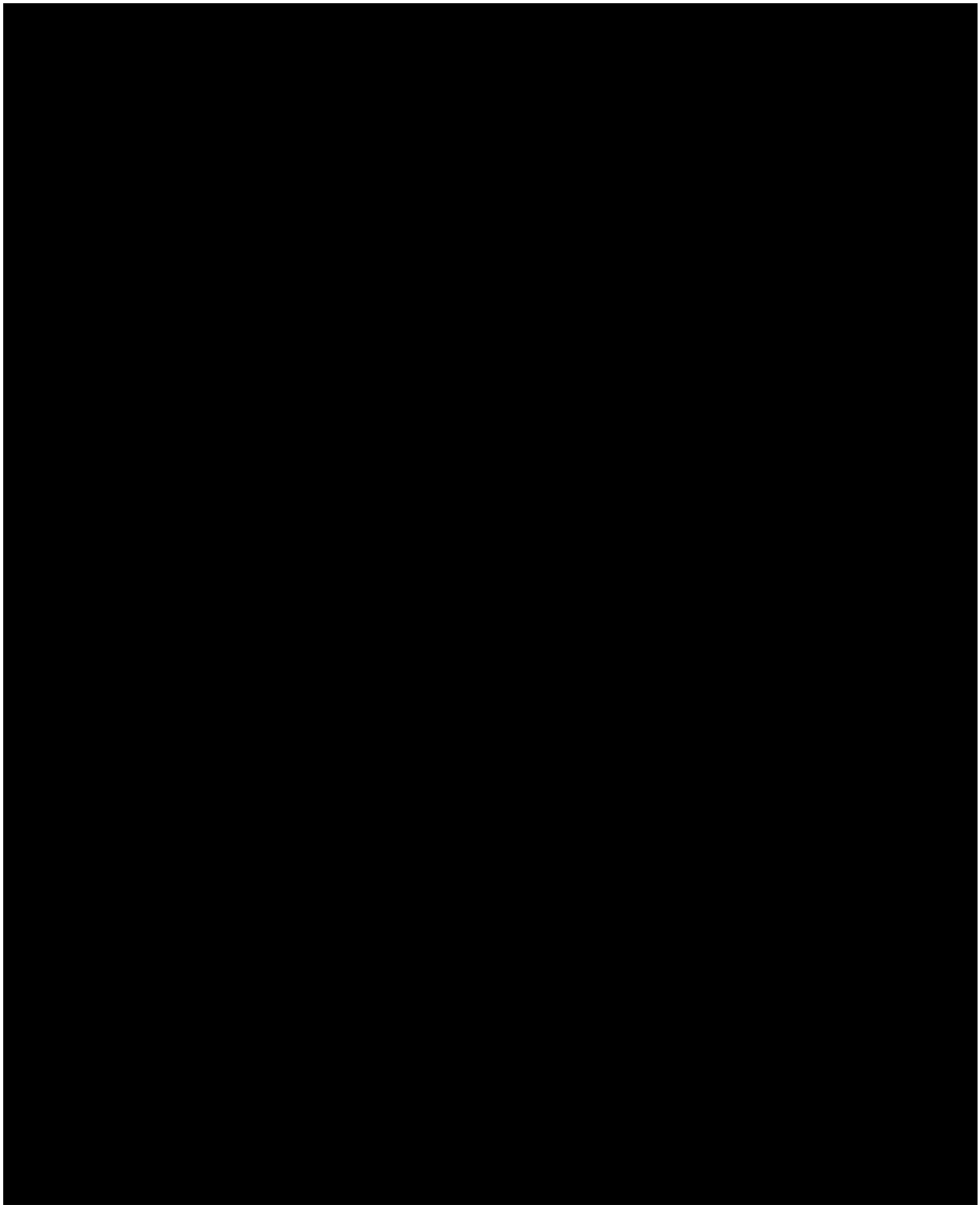

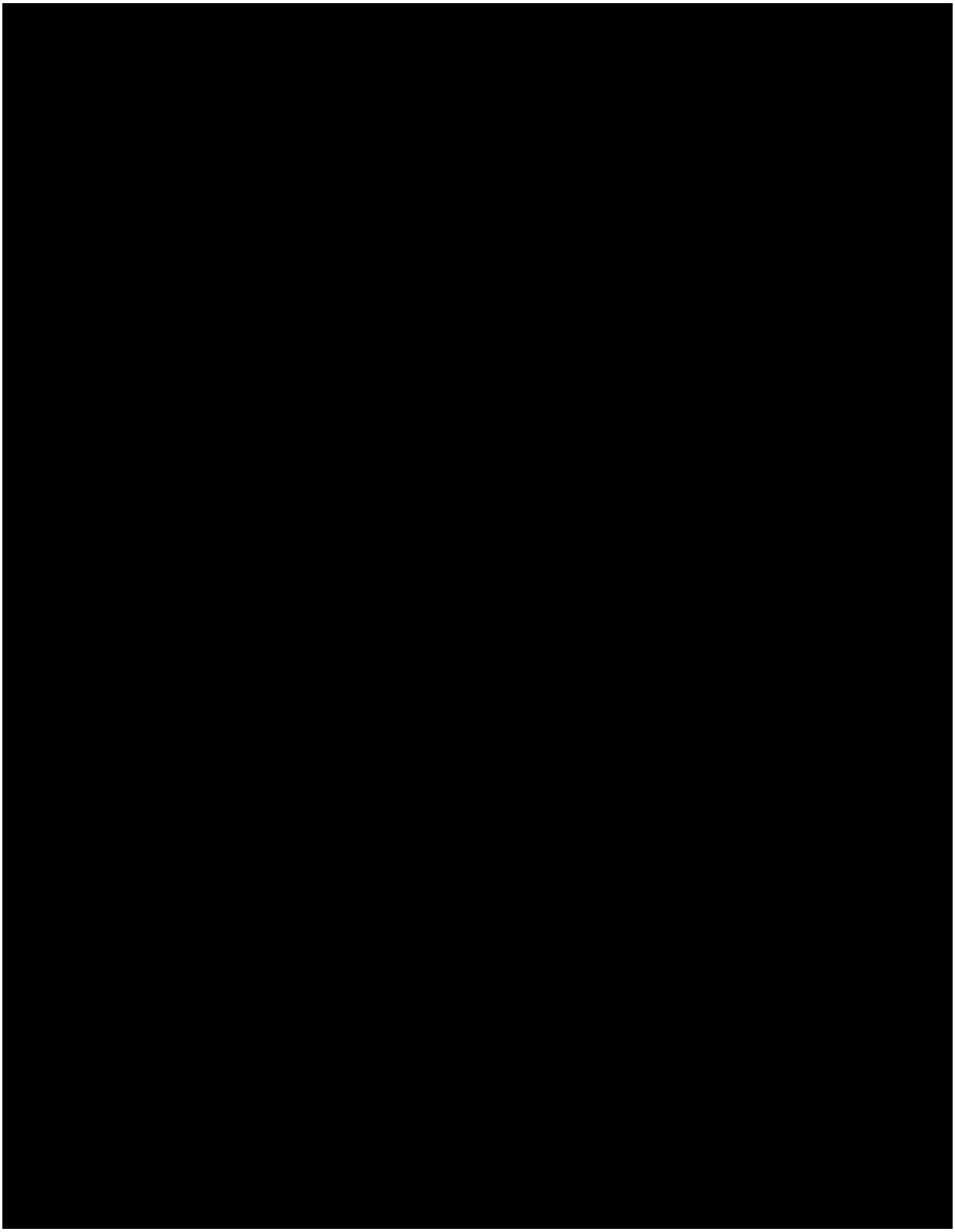

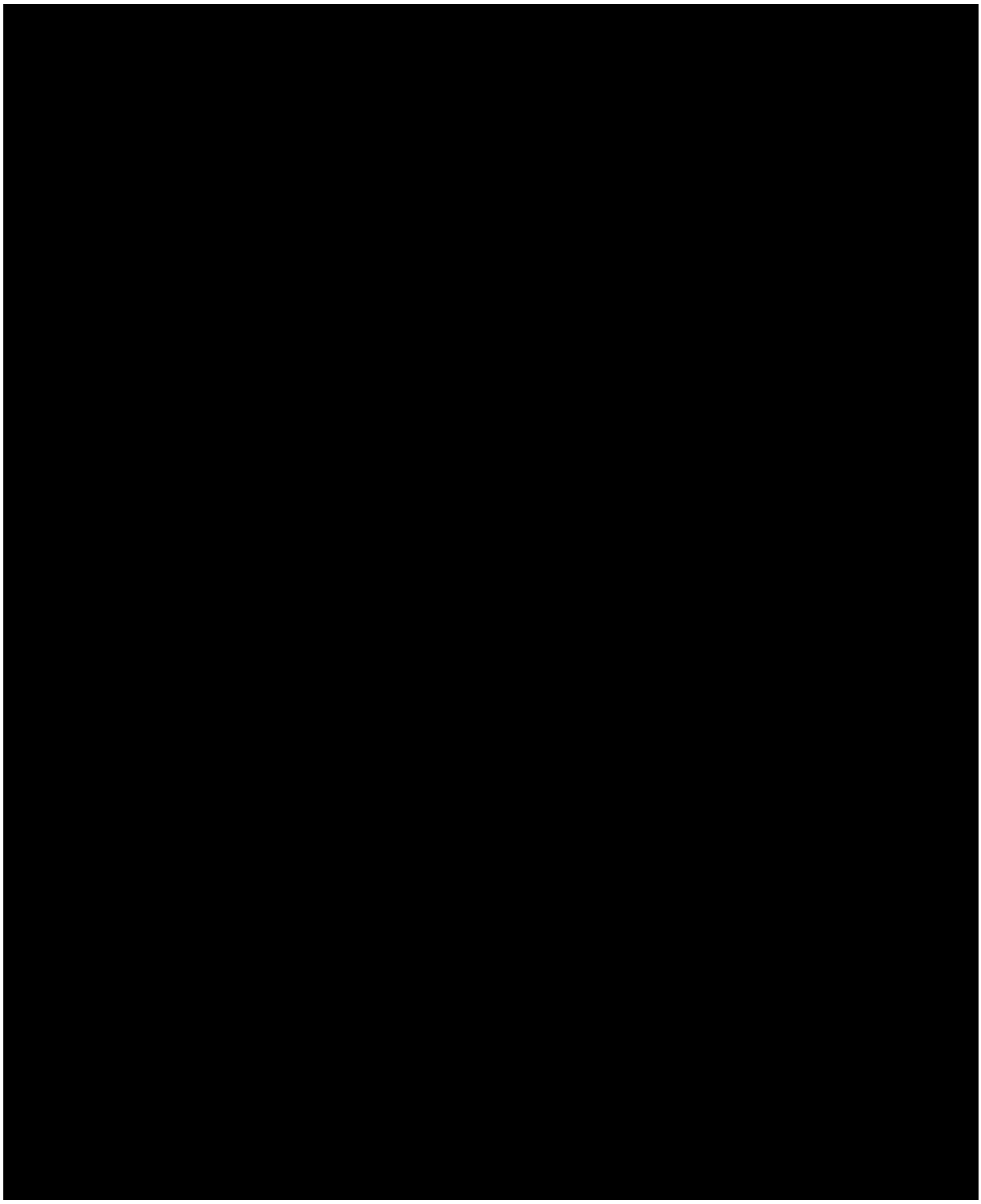

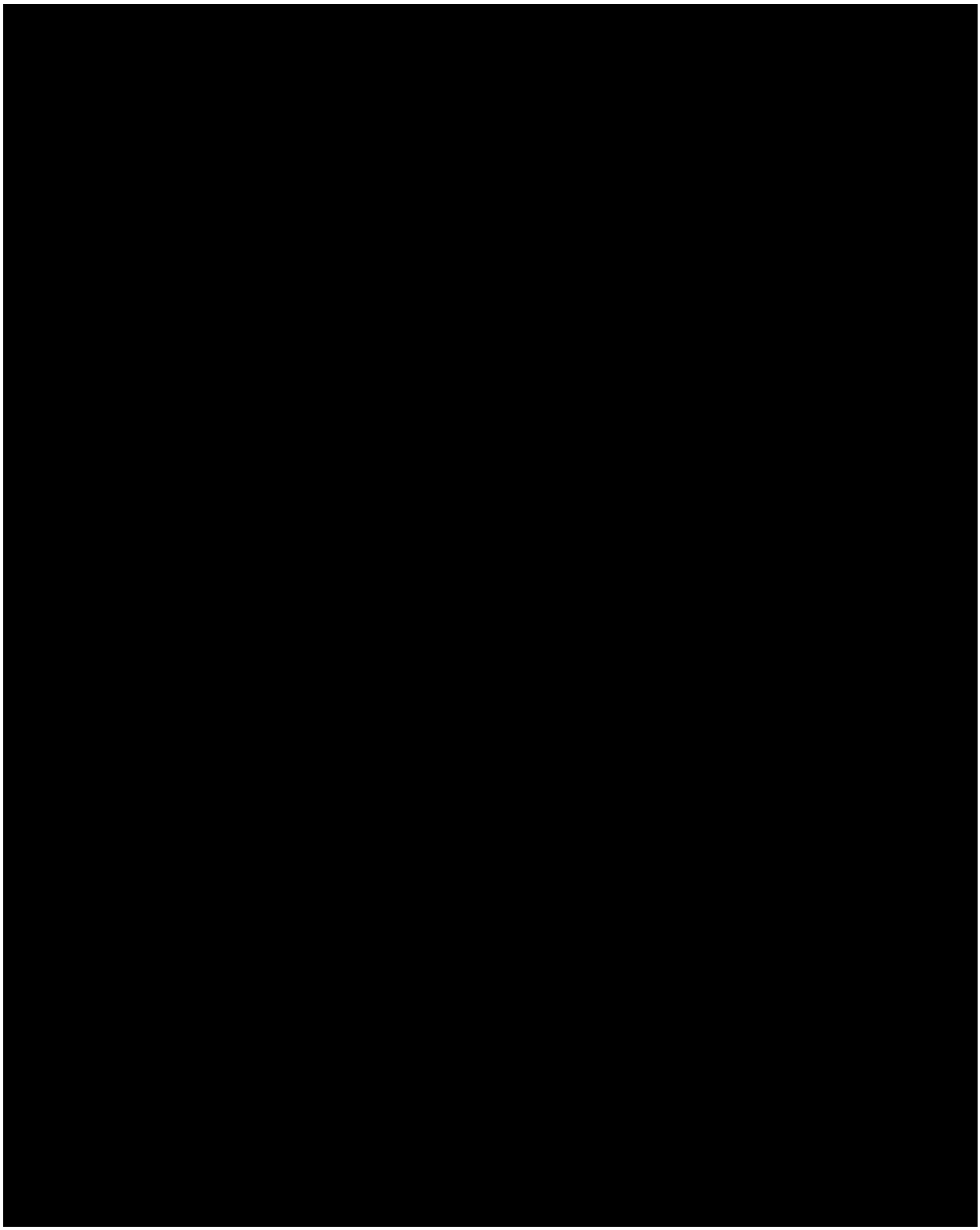

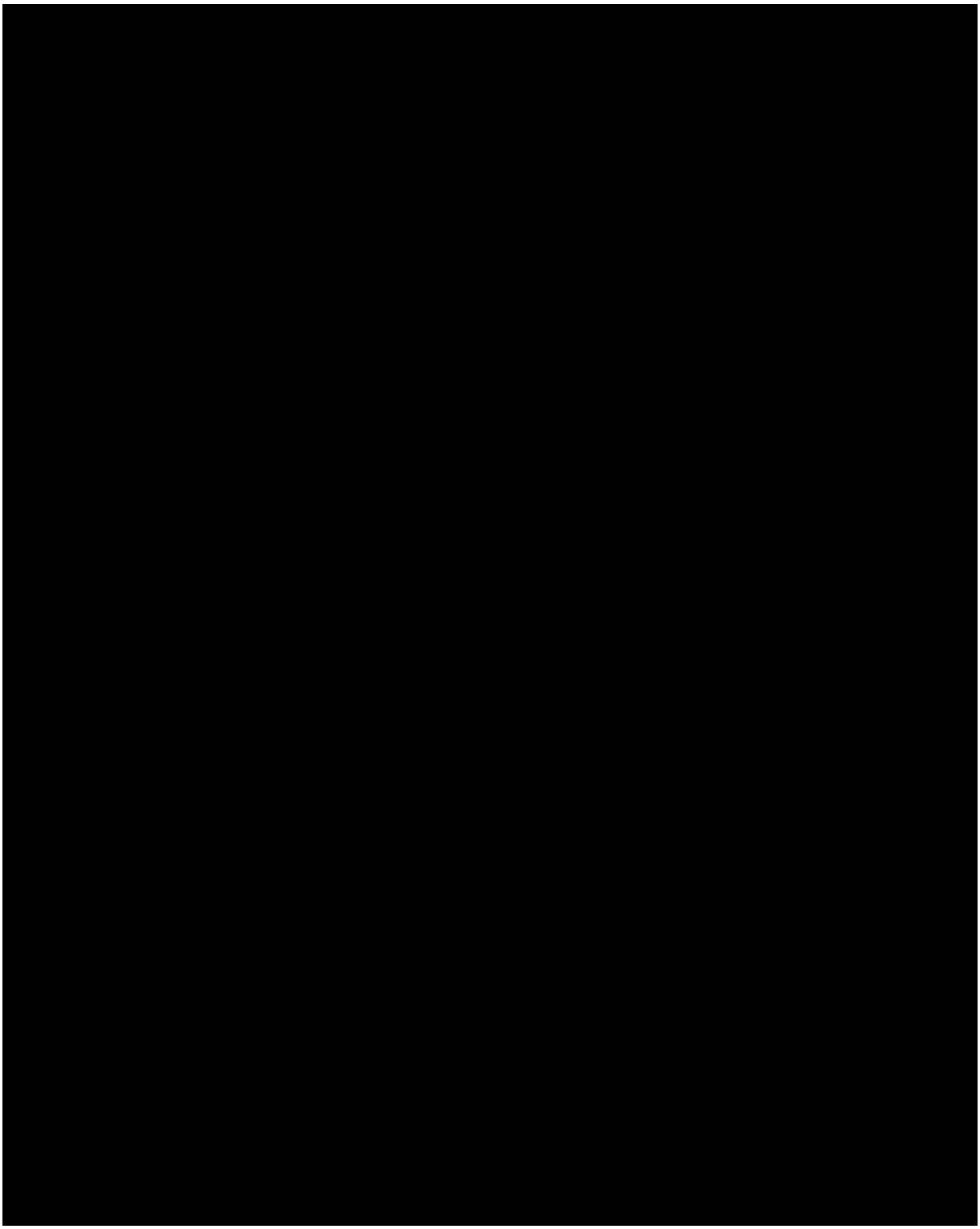

	A	B
1	**Medical Necessity Statement:** We recommend that health care systems should provide medically necessary gender affirming healthcare for transgender and gender diverse people.	
2	Total Responses	88
3	Responses Above 7	78
4	Percent Above 7	89%
5	Percent Below 7	11%
6	Responses Removed	1
7	STATEMENT PASSES	
8		
9	**Primary Care Chapter: Hair Removal Statement:** We recommend that health care professionals refer trans and gender diverse people for hair removal (facial, genital and/or as part of gender affirming surgical intervention) as	
10	Total Responses	88
11	Responses Above 7	77
12	Percent Above 7	88%
13	Percent Below 7	13%
14	Responses Removed	1
15	STATEMENT PASSES	
16		
17	**Sexual Health Chapter:** We recommend health care professionals who provide care to transgender and gender diverse patients discuss the impact of gender affirming treatments on sexual pleasure, function and	
18	Total Responses	89
19	Responses Above 7	85
20	Percent Above 7	96%
21	Percent Below 7	4%
22	Responses Removed	0
23	STATEMENT PASSES	
24		
25	Do you prefer to keep the old version of **Adolescent Chapter Statement 12B**, or do you prefer the new version of **Adolescent Chapter Statement 12B**?	
26	Total Responses	85
27	Old Version	16
28	Percent for Old Version	19%
29	New Version	69
30	Percent for New Version	81%
31		
32	Do you prefer to keep the old version of **Assessment Chapter Statement 3A**, or do you prefer one of the new versions of **Assessment Chapter Statement 3A**?	
33	Total Responses	84
34	Old Version	8
35	Percent for Old Version	10%
36	One of the New Versions	76
37	Percent for One of the New Versions	90%
38		
39	If you prefer one of the new versions of **Assessment Chapter Statement 3A**, please indicate which version you prefer.	
40	Total Responses	79
41	Version 1 ("sustained")	49
42	Percent for Version 1 ("sustained")	62%
43	Version 2 ("persistent")	30
44	Percent for Version 2 ("persistent")	38%

	A	B
1	**Medical Necessity Statement:** We recommend that health care systems should provide medically necessary gender affirming healthcare for transgender and gender diverse people.	Please be aware that if you responded 1-6, in order for your answer to count, you need to provide constructive comments.
2	9	
3	8	
4	8	
5	9	
6	8	
7	9	
8	9	
9	9	
10	9	
11	9	
12	9	
13	9	
14	9	
15	9	
16	9	
17	9	
18	8	
19	9	
20	9	
21	8	

	A	B
22	9	
23	7	
24	7	
25	7	
26	9	
27	9	
28	9	
29	7	
30	9	
31	9	
32	7	Yes, but you need to clarify here or in the accompanying text what is meant by "medically necessary" lest it be argued that well established procedures are 'experimental' or that conversion type therapies should take precedence.
33	1	That health care systems need to provide medically necessary health care is obvious- practically inherent in the term. The statement needs to say that gender affirming care IS medically necessary.

	A	B
34	1	Define medical necessity. My version: We recommend that health care systems should provide medically necessary gender affirming healthcare for transgender and gender diverse people (addition: for treatment of gender dysphoria or to increase gender congruence.)
35	9	
36	8	
37	1	The concept of medical necessity is undefined. This approaches trans healthcare in transmedicalist terms where the underlying justification for provision of gender-affirming medical interventions is assumed to need to be the reduction of suffering/dysphoria, rather than, for example, self-actualization and bodily autonomy. The strategic essentialist approach of using the concept of medical necessity in order to attempt to create access in contexts where there is hostility towards the legitimacy of trans people's genders is ultimately short-sighted. Healthcare systems should provide gender affirming healthcare for transgender and gender diverse people: if someone expresses desire for it and it can be enabled safely and with informed consent, I argue it should be provided.
38	1	
39	6	Hard to score this as a stand alone. Would be much better to have a statement that clearly states that gender affirming health care is medically necessary. As long as we have that, then statement is fine.
40	9	
41	8	
42	1	It is important to be clear about what is meant by medically necessary (e.g., to decrease xyz, to treat xyz, to improve/increase/assist with xyz...)
43	8	
44	9	
45	9	
46	9	

	A	B
47	9	
48	9	
49	9	I would note that given how this is worded this may open people up to denying this care though. Because the way the sentence is written there isn't an equivalency between "medically necessary" and "gender affirming care" and someone could say well...x,y,z hormones or surgery is not "medically necessary." Recommend considering this edit and or really defining how medical necessity should be determined: Original: "We recommend that health care systems should provide medically necessary gender affirming healthcare for transgender and gender diverse people." Proposed edit: "We recommend that health care systems should provide gender affirming healthcare which is medically necessary for transgender and gender diverse people."
50	9	
51	9	
52	9	
53	9	
54	9	
55	9	
56	9	
57	9	
58	9	
59	9	
60	9	
61	9	
62	9	
63	9	
64	8	
65	6	Hard to vote on this statement without seeing a definition of medical necessity - will this be included, and will it be expansive? Otherwise, this statement could be twisted to deny coverage for care (mis)viewed as cosmetic.
66	9	
67	9	
68	8	
69	7	

	A	B
70	9	
71	5	Without context, my only question is how medical necessity is defined in the chapter. This makes a big difference in terms of my comfort with this statement
72	9	
73	9	
74	5	While I agree with this statement, and feel a huge amount of urgency for it to be clear (especially with the US political landscape), I unfortunately think it's meaningless to most health care systems out of context. It's not clear to me what "provide" means -- does that mean have one provider who offers trans care? An outside provider to whom to refer? Provision without coverage? Similarly, the language "medically necessary gender affirming healthcare" is appropriately expansive, but difficult for systems to implement without more concrete guidance. Many systems, for example, already struggle to adequately staff behavioral health services, and may only have hair removal services in specialty cosmetic surgery programs. This is a situation in which the explanatory text and/or a working definition would be much more helpful to me in the Delphi process.
75	6	Hope that there is clear wording somewhere about what "medically necessary gender affirming healthcare" is, as many essential gender affirming healthcare interventions are often deemed not "medically necessary" by medical health insurance providers and state institutions. It would be essential to include a statement somewhere in the chapter that's more affirmative that gender affirming healthcare is generally medically necessary, including but not limited to HRT and surgical interventions like chest reconstruction and genital surgery. Or for this statement to read something like "We recommend that health care systems should provide gender affirming healthcare for transgender and gender diverse people as it is medically necessary /due to it's medical necessity" etc.
76	9	
77	7	

	A	B
78	8	Please define medically necessary in the supporting text
79	9	
80	8	
81	9	
82	7	
83	8	
84	7	
85	9	
86	8	
87	7	
88	8	I wish it could be stated more strongly
89	9	
90		

	C	D
1	**Primary Care Chapter: Hair Removal Statement**: We recommend that health care professionals refer trans and gender diverse people for hair removal (facial, genital and/or as part of gender affirming surgical intervention) as necessary.	Please be aware that if you responded 1-6, in order for your answer to count, you need to provide constructive comments.
2	9	
3	7	
4	8	
5	5	should be a general implementation. In my opinion if is a conduct to cis (aesthetic) and trans comunity will be just.
6	3	Or in preparation of GA surgical intervention
7	9	
8	9	
9	9	
10	9	
11	9	
12	9	
13	9	And facial, genital, and other hair removal (forearm before phalloplasty, body hair when causing dysphoria) should be listed with medically necessary treatments
14	9	
15	9	
16	9	
17	9	
18	9	
19	8	
20	8	
21	8	

	C	D
22	7	
23	7	
24	7	
25	8	
26	9	
27	9	
28	9	
29	7	
30	9	
31	9	
32	7	Yes, but as above, you need to clarify here or in the accompanying text what is meant by "necessary," as this statement allows a lot of wiggle room to argue against coverage. Also, necessity should ultimately be a matter of self declaration.
33	3	Delete "as necessary" - unclear who decides necessity (although it is implied it is someone other than the patient, which is not good). Edit to "OFFER TO refer" so that it cannot be read as a requirement, and the decision ultimately remains the patient's. This is how the voice chapter phrased their statments.

	C	D
34	1	Define necessary. My Version: We recommend that health care professionals refer trans and gender diverse people for hair removal (facial, genital and/or as part of gender affirming surgical intervention) as necessary (addition: for treatment of gender dysphoria or to increase gender congruence.)
35	9	
36	9	
37	9	
38	7	
39	6	Again difficult to score this as it is not clear what constitutes 'as necessary.' Also, awkward wording with the parenthetical in the middle.
40	9	
41	8	
42	8	
43	5	Some words are missing: "We recommend that health care professionals refer trans and gender diverse people for hair removal (facial, genital and/or [MISSING WORDS!] as part of gender affirming surgical intervention) as necessary." Also: Ensure consistency with terminology (trans and gender diverse vs transgender and gender diverse)
44	9	
45	9	
46	9	

	C	D
47	9	
48	9	
49	9	
50	9	
51	9	
52	9	
53	9	
54	9	
55	9	
56	9	Just to confirm in final version whether trans and gender diverse people or transgender and gender diverse people, to be consistent throughout SOC 8.
57	9	
58	9	
59	9	
60	9	
61	9	
62	9	
63	9	
64	9	
65	9	
66	8	
67	8	
68	8	
69	8	

	C	D
70	7	
71	7	
72	5	This statement appears to be incomplete. Also, as I understand it, electrolysis is the mode of hair removal that delivers the most permanent result. Should we not be specifying electrolysis, rather than leaving it open?
73	5	Please consider changing to: "We recommend that health care professionals refer trans and gender diverse people for hair removal (facial, genital and/or as part of gender affirming surgical intervention) as a necessary gender-affirming medical service.
74	3	I feel strongly that HCPs should be able to connect patients with hair removal. However, I also feel strongly that the text should read "as desired" or "as indicated" rather than "as necessary." While hair removal may be recommended by a surgeon for improved outcomes with inversion vaginoplasty, it should not be proactively recommended by health care providers unless a patient expresses hair-related dysphoria. To assume that a patient desires hair removal reveals biases about beauty that are both cisnormative and Eurocentric.
75	1	
76	8	
77	7	

	C	D
78	6	Please include the acknowledgement that most health care professionals do not have ready access to resources/referrals to gender competant hair removal professionals
79	9	
80	8	
81	9	
82	9	
83	7	
84	7	
85	8	
86	7	
87	9	
88	5	Chest and other body hair may be equally as important. Might not need to have specific examples in the statement.
89	9	
90	8	

	E	F
1	**Sexual Health Chapter:** We recommend health care professionals who provide care to transgender and gender diverse patients discuss the impact of gender affirming treatments on sexual pleasure, function and satisfaction.	Please be aware that if you responded 1-6, in order for your answer to count, you need to provide constructive comments.
2	1	In theory this is great but this placed a lot of pressure on the provider in the face of a paucity of evidence. I don't think that we have enough to be able to. I would be in favor of redirecting the statement to include a discussion about sexual function/satisfaction with gender affirming hormone treatment (this leaves room for a "we don't know..." discussion).
3	7	
4	8	
5	8	
6	8	
7	9	
8	9	
9	9	
10	9	
11	9	
12	9	
13	9	
14	9	
15	9	
16	9	
17	9	
18	9	
19	9	
20	9	
21	9	

	E	F
22	9	
23	7	When, in the background text, it would be mentioned that the use of puberty suppression in early puberty would result anorgasmia, I wouldn't agree
24	7	
25	8	
26	9	
27	9	
28	9	
29	8	
30	9	
31	9	
32	1	There is little to no evidence for or against the idea that gender affirming treatments cause negative impacts on sexual pleasure, function and satisfaction. In fact, it may be worth exploring the degree to which they improve it (for instance in terms of comfort with one's body and growth of clitoral tissue). In any case, in the absence of more than anecdotal evidence this statement should be eliminated. As it stands, this statement is almost universally employed by individuals and organizations committed to reducing or eliminating access to transgender healthcare.
33	5	discuss with whom? to what end? Consider making wording parallel to other chapters. example from voice: ... hcp inform TGD people commencing testosterone therapy of the potential and variable effects of this treatment on voice and communication"

	E	F
34	5	This statement feels like it may have arisen from the controversy that Dr. Marci Bowers got herself into when she violated the SOC8 confidentiality agreement by talking with Abigail Shrier. The idea is good but this is the job of medical providers. As a therapist in the US, I always discuss this with regards to endocrine and surgical interventions and so maybe whatever this statement becomes, it should align with the assessment chapter.
35	7	I agree that it is very important to provide information about the 'potential' impacts of gender affirming interventions on sexual pleasure, function and satisfaction. My hope is that the chapter frames this material in a very sex positive manner, including by encouraging trans and gender diverse people to explore how their relationship to their body may change.
36	7	
37	7	It is important that 'impact' equally recognises how the relationship between gender affirming interventions and sexual pleasure, function, and satisfaction can be positive or neutral, and not frame these discussions solely in terms of 'risk'. E.g., improved quality of life or mood as a result of lessened dysphoria may improve sex drive or experiences of sexual activity.
38	7	
39	7	
40	8	
41	8	
42	8	
43	8	
44	9	
45	9	
46	9	

	E	F
47	9	
48	9	
49	9	Recommend adding a comma after "function" and before "and satisfaction." The challenge here is what to discuss? I hope this is addressed in the text.
50	9	
51	9	
52	9	
53	9	
54	9	
55	9	
56	9	
57	9	
58	9	
59	9	
60	9	
61	9	
62	9	
63	9	
64	9	
65	9	
66	9	
67	9	
68	9	
69	9	

	E	F
70	9	
71	9	
72	9	
73	9	
74	9	
75	9	
76	8	
77	8	

	E	F
78	8	
79	9	
80	8	
81	9	
82	9	
83	7	
84	7	
85	9	
86	9	
87	7	
88	7	Important for the text to take into consideration how concerns about long term sexual functioning difficulties have increasingly been used to advocate against youth being able to access puberty suppression. I don't believe there is any actual evidence to suggest this is a common risk and does not appropriately acknowledge that there are many benefits that often outweigh this concern. Encouraging/pressuring someone to explore their sexuality and be sexually active as a prerequisite to pursuing hormone therapy and/or surgery is inappropriate if this is not desired by the young person. Also important that the text highlights the benefits of gender affirming treatment on sexual pleasure, function, and satisfaction.
89	9	
90	9	

	G	H
1	Do you prefer to keep the old version of **Adolescent Chapter Statement 12B**, or do you prefer the new version of **Adolescent Chapter Statement 12B?**	If you don't agree with the change and prefer the Old Version, please explain why below.
2	New Version	
3	New Version	
4	New Version	
5	New Version	
6	New Version	
7	New Version	
8	New Version	I believe criterium d) is worded in a way that can be used to withhold care from trans adolescents with any kind of mental health concern and should be revised. It is unclear to me why the exploration of gender identity issues have to be deprioritised over any other mental health issues when in so many cases they are at the root of mental health concerns, as opposed to the other way around. Why not explore gender identity issues first in case of unclarity?
9	New Version	
10	New Version	
11	New Version	
12	New Version	
13	New Version	
14	New Version	
15	New Version	
16	New Version	
17	New Version	
18	New Version	
19	New Version	
20	New Version	Comment: you should delete the "when" .....
21	New Version	

	G	H
22	New Version	
23	Old Version	I would vote for a combination; when there is experience of gender diversity / incongruence of several years. Also, sustained is not so strong as persistent, so I rather have persistent if the new version is used.
24	Old Version	Consistent text with WHO ICD 11
25	Old Version	The definition of persistence indicates an existence of an experience over a prolonged period of time, where as sustained suggests that there may be some interruption to the experience, which may not always be the case
26	Old Version	Saying "marked and sustained" leaves it too open to interpretation. We are seeing too many young people approved for medical treatment with little or no efforts at diagnosis beyond the youth declaring an identity.
27	Old Version	I feel the old version gives providers more direct guidance and helps prevent young people transitioning too quickly (which could result in later regret).
28	Old Version	Define sustained
29	Old Version	The field is heavily under fire in this area, and I do not believe the change suggested is supported by the data.
30	Old Version	The old version is aligned with WHO definition - and that is our best defense.
31	New Version	This is a very serious and NECESSARY change.
32	New Version	
33	New Version	

	G	H
34	New Version	
35	New Version	
36	New Version	
37	New Version	
38	New Version	
39	New Version	I don't love the words marked and sustained
40	New Version	
41	New Version	
42	New Version	
43	New Version	
44	New Version	
45	New Version	
46	New Version	

	G	H
47	New Version	
48	New Version	
49	New Version	
50	New Version	
51	New Version	
52	New Version	
53	New Version	
54	New Version	
55	New Version	
56	New Version	
57	New Version	
58	New Version	
59	New Version	
60	New Version	
61	New Version	
62	New Version	
63	New Version	
64	New Version	
65	New Version	
66	New Version	
67	New Version	
68	New Version	
69	New Version	

	G	H
70	New Version	
71	New Version	
72	New Version	
73	New Version	Several years is unethical - it could withhold lifesaving treatment. Also the idea that someone has to prove "several years" or "since early childhood" is a colonial, racist idea. Also strongly consider removing "only" after "should only" - this wording makes it sound like providers need to be in fear or overly cautious. Just writing "should" suffices.
74	New Version	
75	New Version	
76	Old Version	There should be more caution around adolescents.
77	Old Version	The studies thus far provide evidence for recommending medical and surgical treatments in youth with sustained gender incongruence (i.e. several years). I am okay with the use of sustained, but believe it is good to indicate that that means several years.

	G	H
78	Old Version	I think either version is acceptable, provided "several years" or "marked and sustained" is better defined in the text. If I would err, though I would err on the side of at least 1 year of sustained gender diversity, rather than a marked and sustained but only over 3 months.
79	Old Version	Sustained is too vague
80	New Version	
81	New Version	
82	New Version	
83	Old Version	What does "marked and sustained" mean? If these are supposed to be guidelines written by the experts in the field, we need to provide more concrete guidance. Hormone treatments are being prescribed by many people now, without much expertise.
84	Old Version	"Marked and sustained" are both undefined and, thereby, allow totally arbitary interpretations.
85	Old Version	
86	Old Version	Documentation especially important in adolescents. In most cases such documentation should come from an independent source usually a supportive parent. Besides how does one measure or document " marked and sustained" without independent sources. Both 12A and 12 B are not mutually exclusive except that 12B has the potential to laid the burden solely on the adolescent.
87		
88		
89		
90		

	I	J
1	Do you prefer to keep the old version of **Assessment Chapter Statement 3A**, or do you prefer one of the new versions of **Assessment Chapter Statement 3A?**	If you don't agree with the change and prefer the Old Version, please explain why below.
2	One of the New Versions (Vote Below)	
3	One of the New Versions (Vote Below)	
4	One of the New Versions (Vote Below)	
5	One of the New Versions (Vote Below)	
6	One of the New Versions (Vote Below)	
7	One of the New Versions (Vote Below)	
8	One of the New Versions (Vote Below)	
9	One of the New Versions (Vote Below)	
10	One of the New Versions (Vote Below)	
11	One of the New Versions (Vote Below)	
12	One of the New Versions (Vote Below)	
13	One of the New Versions (Vote Below)	
14	One of the New Versions (Vote Below)	
15	One of the New Versions (Vote Below)	
16	One of the New Versions (Vote Below)	
17	One of the New Versions (Vote Below)	
18	One of the New Versions (Vote Below)	NEW VERSION 2
19	One of the New Versions (Vote Below)	
20	One of the New Versions (Vote Below)	
21	One of the New Versions (Vote Below)	

	I	J
22	One of the New Versions (Vote Below)	
23	One of the New Versions (Vote Below)	
24	One of the New Versions (Vote Below)	Version 2 Consistent text with WHO ICD 11
25	One of the New Versions (Vote Below)	
26	One of the New Versions (Vote Below)	
27	One of the New Versions (Vote Below)	
28	One of the New Versions (Vote Below)	New version 2
29	Old Version	I do not see the science behind this suggested change.
30	Old Version	The old version is aligned with WHO definition - and that is our best defense.
31		I don't care about sustained vs. persistent. I personally feel strongly that the statement 3A shouldn't be there at all.
32	One of the New Versions (Vote Below)	
33	One of the New Versions (Vote Below)	

	I	J
34	One of the New Versions (Vote Below)	
35	One of the New Versions (Vote Below)	
36	One of the New Versions (Vote Below)	
37	One of the New Versions (Vote Below)	
38	One of the New Versions (Vote Below)	
39	One of the New Versions (Vote Below)	
40	One of the New Versions (Vote Below)	
41	One of the New Versions (Vote Below)	
42	One of the New Versions (Vote Below)	
43	One of the New Versions (Vote Below)	
44	One of the New Versions (Vote Below)	
45	One of the New Versions (Vote Below)	
46	One of the New Versions (Vote Below)	

	I	J
47	One of the New Versions (Vote Below)	
48	One of the New Versions (Vote Below)	
49	One of the New Versions (Vote Below)	
50	One of the New Versions (Vote Below)	
51	One of the New Versions (Vote Below)	
52	One of the New Versions (Vote Below)	I actually like the language 'persistent' better than 'sustained' but I think the language between adolescents and adults should be the same. So whichever is used, they should be the same so as to avoid confusion.
53	One of the New Versions (Vote Below)	
54	One of the New Versions (Vote Below)	
55	One of the New Versions (Vote Below)	
56	One of the New Versions (Vote Below)	
57	One of the New Versions (Vote Below)	
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61	One of the New Versions (Vote Below)	
62	One of the New Versions (Vote Below)	
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66	One of the New Versions (Vote Below)	
67	One of the New Versions (Vote Below)	
68	One of the New Versions (Vote Below)	
69	One of the New Versions (Vote Below)	

	I	J
70	One of the New Versions (Vote Below)	
71	One of the New Versions (Vote Below)	
72	One of the New Versions (Vote Below)	
73	One of the New Versions (Vote Below)	Sustained is better than persistent. How about take out "Only" and just write "recommend"?
74	One of the New Versions (Vote Below)	
75	One of the New Versions (Vote Below)	
76	One of the New Versions (Vote Below)	This statement does not have to match the adolescent statement because adult and adolescent experiences are not exactly the same due to developmental concerns with adolescents.
77	One of the New Versions (Vote Below)	

	I	J
78	One of the New Versions (Vote Below)	Version 1 (marked and sustained) is preferred, but this phrase should be more fully defined in the text. The gender incongruence/diversity need not be documented, but should have some clear historical duration beyond a few months
79	One of the New Versions (Vote Below)	
80		
81	Old Version	
82	Old Version	
83	Old Version	same comment as above
84	Old Version	Both "marked and sustained" and "marked and persistent" are open to any interpretation, plus both new versions have given up on the documentation requirement and "local contexts", which adds to their weakness.
85	Old Version	
86	Old Version	Surgery in a serious intervention as is hormonal treatment. It needs to be documented for surgery that the person has lived on hormones and in the preferred gender.
87		
88		
89		
90		

	K	L
1	If you prefer one of the new versions of **Assessment Chapter Statement 3A**, please indicate which version you prefer.	
2	Version 2 ("persistent")	
3	Version 2 ("persistent")	
4	Version 2 ("persistent")	
5	Version 2 ("persistent")	
6	Version 2 ("persistent")	
7	Version 2 ("persistent")	
8	Version 2 ("persistent")	
9	Version 2 ("persistent")	
10	Version 2 ("persistent")	
11	Version 2 ("persistent")	
12	Version 2 ("persistent")	
13	Version 2 ("persistent")	
14	Version 2 ("persistent")	
15	Version 2 ("persistent")	
16	Version 2 ("persistent")	
17	Version 2 ("persistent")	
18	Version 2 ("persistent")	
19	Version 2 ("persistent")	
20	Version 2 ("persistent")	
21	Version 2 ("persistent")	

	K	L
22	Version 2 ("persistent")	
23	Version 2 ("persistent")	
24	Version 2 ("persistent")	
25	Version 2 ("persistent")	
26	Version 2 ("persistent")	
27	Version 2 ("persistent")	
28	Version 2 ("persistent")	
29	Version 2 ("persistent")	
30	Version 2 ("persistent")	
31	Version 2 ("persistent")	
32	Version 1 ("sustained")	
33	Version 1 ("sustained")	

	K	L
34	Version 1 ("sustained")	
35	Version 1 ("sustained")	
36	Version 1 ("sustained")	
37	Version 1 ("sustained")	
38	Version 1 ("sustained")	
39	Version 1 ("sustained")	
40	Version 1 ("sustained")	
41	Version 1 ("sustained")	
42	Version 1 ("sustained")	
43	Version 1 ("sustained")	
44	Version 1 ("sustained")	
45	Version 1 ("sustained")	
46	Version 1 ("sustained")	

	K	L
47	Version 1 ("sustained")	
48	Version 1 ("sustained")	
49	Version 1 ("sustained")	
50	Version 1 ("sustained")	
51	Version 1 ("sustained")	
52	Version 1 ("sustained")	
53	Version 1 ("sustained")	
54	Version 1 ("sustained")	
55	Version 1 ("sustained")	
56	Version 1 ("sustained")	
57	Version 1 ("sustained")	
58	Version 1 ("sustained")	
59	Version 1 ("sustained")	
60	Version 1 ("sustained")	
61	Version 1 ("sustained")	
62	Version 1 ("sustained")	
63	Version 1 ("sustained")	
64	Version 1 ("sustained")	
65	Version 1 ("sustained")	
66	Version 1 ("sustained")	
67	Version 1 ("sustained")	
68	Version 1 ("sustained")	
69	Version 1 ("sustained")	

	K	L
70	Version 1 ("sustained")	
71	Version 1 ("sustained")	
72	Version 1 ("sustained")	
73	Version 1 ("sustained")	
74	Version 1 ("sustained")	
75	Version 1 ("sustained")	
76	Version 1 ("sustained")	
77	Version 1 ("sustained")	

	K	L
78	Version 1 ("sustained")	
79	Version 1 ("sustained")	
80	Version 1 ("sustained")	
81		
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84		
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Re: International advisory - confidential

From: Eli Coleman <dreli[redacted]
To: walterbouman <walterbouman[redacted]
Cc: asa.radix[redacted], jgreen <jgreen[redacted], gail.knudson[redacted], Jon Arcelus <[redacted], marcib[redacted], Vin Tangpricha [redacted]
Date: Sat, 21 Aug 2021 14:43:07 -0400

Besides, my belief that this is the right thing to do, I would be concerned what commitments have made to our international advisory committee.

Eli

On Sat, Aug 21, 2021 at 1:29 PM Walter Bouman <walterbouman[redacted] wrote:

> Dear Eli,
>
> Thanks for your thoughts. What was agreed in the past, may be obsolete in the present. We will discuss this in the Board and get back to you; and i will check what Rachel Levine's point of view is on these issues, when I meet with her next week.
> The sooner the SOC8 is published, the better, as it will potentially significantly improve the lives of millions of trans people and their families globally.
>
> Best,
>
> Walter
>
> Dr Walter Pierre Bouman MD MA MSc UKCPreg PhD
>
> Consultant in Trans Health/Hon. Professor School of Medicine, University of Nottingham, United Kingdom
>
> President World Professional Association for Transgender Health (WPATH)
>
> Editor-in-Chief International Journal of Transgender Health(IF = 5.333)
>
> Nottingham National Centre for Transgender Health
>
> [redacted]

> On 21 Aug 2021, at 15:47, Eli Coleman <dreli@[redacted] wrote:
>
> We had agreed long ago that we would send to the International advisory committee and for legal review.
>
> Eli
>
> On Sat, Aug 21, 2021 at 2:18 AM Walter Bouman <walterbouman[redacted] wrote:
> Okay, lets discuss this in more dept at some point as to which organization to ask to review the SOC8 and with which aim; how this fits in the current timeline; what to do if an organization objects to certain sections/Delphi statements of the SOC8.
>
> The SOC8 are clinical guidelines, based on clinical consensus and the latest evidenice based medicine; i dont recall the Endocrine Guidelines going through legal reviews before publication, or indeed the current SOC?
>
> With warm wishes and stay safe,
>
> Walter
>
> Dr Walter Pierre Bouman MD MA MSc UKCPreg PhD
>
> Consultant in Trans Health/Hon. Professor School of Medicine, University of Nottingham, United Kingdom
>
> President World Professional Association for Transgender Health (WPATH)
>
> Editor-in-Chief International Journal of Transgender Health(IF = 5.333)
>
> Nottingham National Centre for Transgender Health
>
> [redacted]
>
> [redacted]
>
> > On 20 Aug 2021, at 23:03, Asa Radix <asa.radix[redacted] wrote:

You are correct Eli. He had a lot of work going on and I don't see an ethical issue

On Fri, Aug 20, 2021, 5:39 PM Eli Coleman <dreli[redacted]> wrote:
First of all, I only recall that [redacted] removed himself because he was not able to keep up with the demands - so I don't know what the ethical issue is.

Second, I don't know that you can simply select a board member of GATE to be the representative. It seems that [redacted] would be the one to decide who would review for GATE.

And, it is clearly important for GATE to review.

Eli

On Fri, Aug 20, 2021 at 4:30 PM Jamison Green <jgreenp[redacted]> wrote:
I agree with Asa. GATE must be included, even if it's not [redacted]. Isn't [redacted] affiliated with GATE now, too? And we did ask [redacted] (thank you, Asa, for reminding me of his last name!), too, early on, so I would like to have him take a look from this perspective, apart from his role on the Global chapter, if at all possible.

And a US legal (broad) review will be necessary because sometimes a human rights approach conflicts with the civil rights available to trans people and providers in the US. We should at least be aware of any conflicts in that area, even if the SOC content doesn't change to accommodate it, because we will have to argue it in court at some point. We should know what those potentially problematic items are before we publish.

Thanks,
Jamison

On Fri, Aug 20, 2021 at 11:30 AM Asa Radix <asa.radix[redacted]> wrote:
We need to include GATE. We could ask that [redacted] be the representative.

Asa

On Fri, Aug 20, 2021, 2:08 PM Walter Bouman <walterbouman[redacted]> wrote:

Dear All,

I seriously think that [redacted] position is compromised as he stepped out of the SOC8 member group, and I seriously struggle - from an ethical position - to see how he can offer a neutral point of view towards WPATH's SOC8.

My thoughts are to ask for a legal (broad) review regarding basic human rights (within reason; so you have to think this through who you ask, otherwise the SOC8 will never see the light of day); and if there is a specific appetite for an US based approach, we can look into this too.....

and then have a global open, on-line consultation period for a few weeks - very similar to the ICD-11 process - and then - assuming there are no very contentious issues emerging - move to publish.

Interested to hear your thoughts.

With warm wishes,

Walter

Dr Walter Pierre Bouman MD MA MSc UKCPreg PhD

Consultant in Trans Health/Honorary Professor School of Medicine, University of Nottingham, UK

President World Professional Association for Transgender Health (WPATH)

Editor-in-Chief *International Journal of Transgender Health* (Impact Factor 2020 = 5.333)

Nottingham National Centre for Transgender Health

[redacted]

On 2021-08-20 03:26, G Knudson wrote:

Hi Eli,

[redacted]

Gail

On Fri, Aug 20, 2021 at 5:38 AM Eli Coleman <dreli[redacted] wrote:

Who is on the international advisory to review the statements in advance of the public period of comment on the SOC?

Thanks!

Eli
--

Eli Coleman, PhD.
Academic Chair in Sexual Health
Professor and Director
The Institute for Sexual and Gender Health
University of Minnesota Medical School
Family Medicine and Community Health
sexualhealth.umn.edu

--

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Fwd: FW: Letter to WPATH re SoC8 Methods

From: Eli Coleman <dreli[redacted]
To: asa.radix[redacted], Jon Arcelus <jon.arcelus[redacted]
Date: Wed, 13 Oct 2021 09:10:29 -0400
Attachments: Wilson 2015.pdf (237.32 kB)

For discussion Friday.

---------- Forwarded message ---------
From:[redacted]
Date: Wed, Oct 13, 2021 at 7:30 AM
Subject: FW: Letter to WPATH re SoC8 Methods
[redacted]

Hi

Maybe I had the wrong email for you? I would be very grateful for a response to our email below

Very many thanks

[redacted]

[redacted]

From: [redacted]
Sent: 30 September 2021 16:56
[redacted]
Subject: FW: Letter to WPATH re SoC8 Methods

Dear Professor Eli Coleman

I was one of the UK government's first LGBT health advisors. My academic profile is here [redacted]. My expertise lies in systematic reviewing, especially regarding sexual and gender minority health topics and for guideline development. I lead a team of researchers who are committed to helping people live their best lives using highest quality & evidence-based healthcare advice.

We published this paper examining all international guidelines in the entire field of transgender health. The work was presented at both the WPATH 2020 and Endosoc 2021 conferences. It has garnered nearly 5000 views & 1000 PDF downloads and no dispute of the findings. We believe the community, health-care practitioners and WPATH want, and need, the next Standards of Care to be better; high-quality, unassailable and deserving of respect by peers across medical disciplines and international bodies. We hoped to be able to report on Appraisal of Guidelines for Research and Evaluation (AGREE II) scores relevant to future guidelines in trans health as they are produced or reissued, and to be able to document improvements in quality. Thus, we await the forthcoming SoC8 with interest. We apologise for not writing sooner as we'd not seen the proposed methods until recently.

We commend WPATH for the explicit aspiration for SoC8 to become evidence-based. Transparent, pre-publication of the Methods is welcome albeit incomplete. We have made a detailed analysis which we are happy to share as previous problems around evidence-based processes and content seem to remain unaddressed. In it we concentrate on a number of key areas, as delineated by [redacted] (attached) that include:

- Guideline panel

- Publicly available protocol
- How the committee gathered the evidence
- Recommendations and the supporting evidence
- External peer review

We would like to engage in dialogue, as there appear to be shortcomings in all the above areas, and weaknesses will leave WPATH SOC8 open to criticism. AGREE II would provide a good remedy. Also I attach a paper about how to make guidelines when the evidence is weak, which I hope might be useful.

Thank you in advance for acknowledging this communication and considering setting up a meeting.

Sincerely,

[redacted]

-- Please click here to view our e-mail disclaimer [redacted]

--

Eli Coleman, PhD.
Academic Chair in Sexual Health
Professor and Director
The Institute for Sexual and Gender Health
University of Minnesota Medical School
Family Medicine and Community Health
sexualhealth.umn.edu

Meetings

From: Jon Arcelus [redacted]
To: Asa Radix [redacted] Eli Coleman [redacted]
Cc: [redacted]
Date: Thu, 18 Nov 2021 10:18:37 -0500

Thanks Asa, I cant do tomorrow as I am in a conference. I am in an away day next Thursday in London too and flying to Spain for a week off on the 26th of November, back on the 6th of December but going back to London on the 9th of December again for my birthday celebration so not sure when I will be able to join you next. I can join you to say hello on the 2nd from Spain.

I will look at many chapters as I can today and next week and look at Eli's comments regarding assessment.

It does look like we will be unable to put the SOC for public comments next week, still waiting for child and surgery from my end and have not read PC, that will take us close to Christmas for public comments which is never a good time. So if we are not doing Public comments till January we will have to look at comments we receive at the end of January. I am disappearing from the face of the earth again from middle January till end of February but could do a bit of work when I am away. I say all that as we mentioned to Rachel that we will have soc ready end of 2021 but it is more likely to be spring 2022, really...

Hope Eli is having a great time in Puerto Rico…would love to have some margaritas in the sun now
Regards
Jon

Prof. Jon Arcelus Alonso, MD, PhD
Professor (Full) of Mental Health and Wellbeing

Honorary Professor Shanghai Jiao Tong University, Shanghai, China.

Honorary Consultant in Transgender Health
Associate Editor of the International Journal of Transgender Health (IF 5.33)
Co-Chair of the Standards of Care 8th Edition (World Professional Association of Transgender Health-WPATH)

Academic Address:
[redacted]

Clinical Address:
[redacted]

[redacted]

From: Asa Radix [redacted]
Date: Thursday, 18 November 2021 at 14:19
To: Jon Arcelus <[redacted] Eli Coleman <[redacted]
Subject: Re: Primary Care chapter and concerns about the Assessment chapter

This Message was Encrypted.

Eli is traveling and I am in a half day meeting. I could talk tomorrow I will also review primary care today. I would like to send terminology to Jun when you are done if there are only minor edits.

Asa

From: Jon Arcelus [redacted]
Sent: Thursday, November 18, 2021 8:04 AM
To: Asa Radix [redacted] Eli Coleman <[redacted]
Subject: Re: Primary Care chapter and concerns about the Assessment chapter

Do I have primary care, assessment, eunuch and terminology to look at? I am surprised about the primary care chapter asking to have a mental health professional in charge of the assessment in adults, is that what she is suggesting? That was the proposal presented in BA which anger a lot of people...unless I understood it wrong...are we talking later?

Prof. Jon Arcelus Alonso, MD, PhD

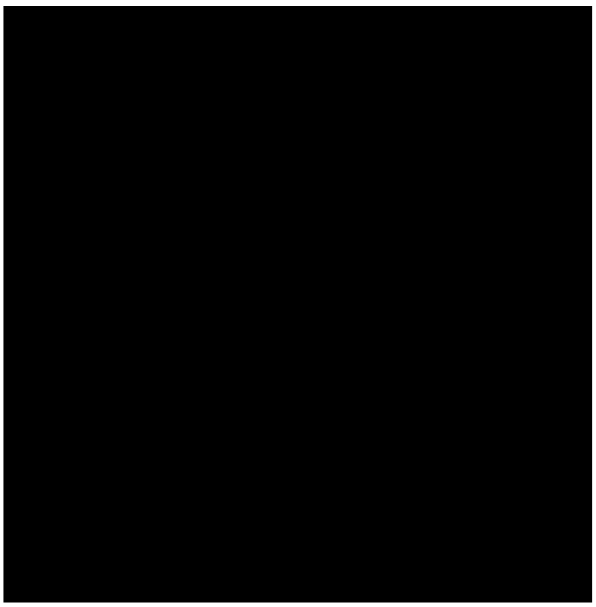
Professor (Full) of Mental Health and Wellbeing

Honorary Professor Shanghai Jiao Tong University, Shanghai, China.

Honorary Consultant in Transgender Health

Associate Editor of the International Journal of Transgender Health (IF 5.33)

Co-Chair of the Standards of Care 8th Edition (World Professional Association of Transgender Health-WPATH)



From: Asa Radix
Sent: 16 November 2021 2:13 PM
To: Jon Arcelus ; Eli Coleman
Subject: Fw: Primary Care chapter and concerns about the Assessment chapter

This Message was Encrypted.

please can you add attached to primary care in shared drive. Jon and Eli, see Maddie's concerns about assessment.
I'll make the first pass and will work on this today.

Asa

From: Deutsch, Madeline
Sent: Tuesday, November 16, 2021 3:17 AM
To: Asa Radix
Cc: Deutsch, Madeline ; Eli Coleman ; jon.arcelus <jon.arcelus
Subject: Primary Care chapter and concerns about the Assessment chapter

Hi Asa,

Please attached revised chapter. There are still some loose ends but we are close.

The loose ends and action plans are described in the comment box at the top. Furthermore, I would like to make minor wording changes for semantics to 3 of the statements, see comments in the text.

Because there have been several steps along the way where guidance on this chapter from the editors has changed, rendering hours of work done by the author team no longer included in the document, I will await specific and clear written feedback from the editors before putting in any additional effort on this chapter, with the exception of the introduction, which I will continue to work on while the document is under editorial review.

As far as a companion paper, I could see one being submitted that discusses competencies, primary care in the global context, behavioral health, and sexual health/sensitive exams. That is not something I will be able to take on until the work on this chapter in SOC8 is complete.

Also as I expressed to you today, I think that having the SOC8 be primarily focused on explanatory statements for the approved delphi statements is a misguided approach. Many clinical practice guidelines, including for example the Endocrine Society Guidelines, expand in detail on a range of relevant matters outside of explanatory text for recommendation statements. Furthermore, most of the recommendation statements in SOC8 are not PICO format but consensus based or based on weak evidence. So it seems somewhat arbitrary to exclude other very important information and topics. This once-in-a-decade opportunity to get on the record about critical issues in transgender health should not be hamstrung by this restrictive outlook, in my view. A perfect example is the exclusion from SOC7 of a clear statement of medical necessity, which required the 2016 clarification statement - a statement often overlooked or outright dismissed by health ministries or insurance payers as "not part of the actual SOC".

Lastly, I wanted to emphasize the concerns I raised regarding the assessment chapter's statement that the guideline for surgery access will be a "suggested" 6 months of hormone therapy prior to permanent and sterilizing genital and gonadal procedures, as well as the general lax approach to criteria for surgical care in general. In my view and experience this is very inappropriate and will have several very negative effects. First, it will place any provider of any discipline who identifies any need for caution, pause, or further exploration and identity integration prior to moving forward with these surgeries to become a gatekeeper in the eyes of the patient. Second, it will fuel already opportunistic and in some cases predatory practices by some surgeons in this field, who will be emboldened as well as enabled by a removal of any waiting period. Third, it will cause confusion and frustration for payers who are growing increasingly concerned with a lack of clear guidelines and regulation in this area, particularly in the case of subjective interventions such as breast augmentation revisions or FFS (see also - the Q and A sessions for the numerous GEI insurance trainings I and others have participated in in recent months - these themes were a primary focus of this morning's session). Fourth, and most concerningly, this will absolutely and without question fuel the political pushback in

the US and elsewhere by those who claim that there is a transgender medicine-industrial complex that is ripe with conflicts of interest and intent on pushing forward gender transition related care in all cases without regulation or introspection.

The way the chapter is currently worded, there is no requirement that the assessing provider for surgery be a mental health clinician, nor have any other specific qualifications or benchmark to conduct this assessment. This will shift the burden of "forced gatekeeper" onto PCPs and other medical providers. In fact, will a surgeon themself be able to do the assessment if they so deem themself as qualified to do so? I am absolutely certain that, should this content remain as-is, within weeks of SOC8 release, there will be scores of new grad primary care nurse practitioners and PAs, who have completed 2 years of masters level training, identifying themselves as qualified to make these assessments and opening up the tap to what is effectively surgery on demand. This will certainly backfire and cause great difficulties for access to and coverage for this care, and harm to the reputation and level of respect for WPATH and its SOC. There is a middle way forward that rejects the restrictions and barriers of prior years, yet maintains quality and sets standards and expectations that are appropriate for good patient care and government and payer policies.

Best,

Maddie

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Maddie Deutsch, MD, MPH
Medical Director, UCSF Gender Affirming Health Program
Associate Professor of Clinical Family & Community Medicine
University of California - San Francisco

President-Elect, US Professional Association for Transgender Health

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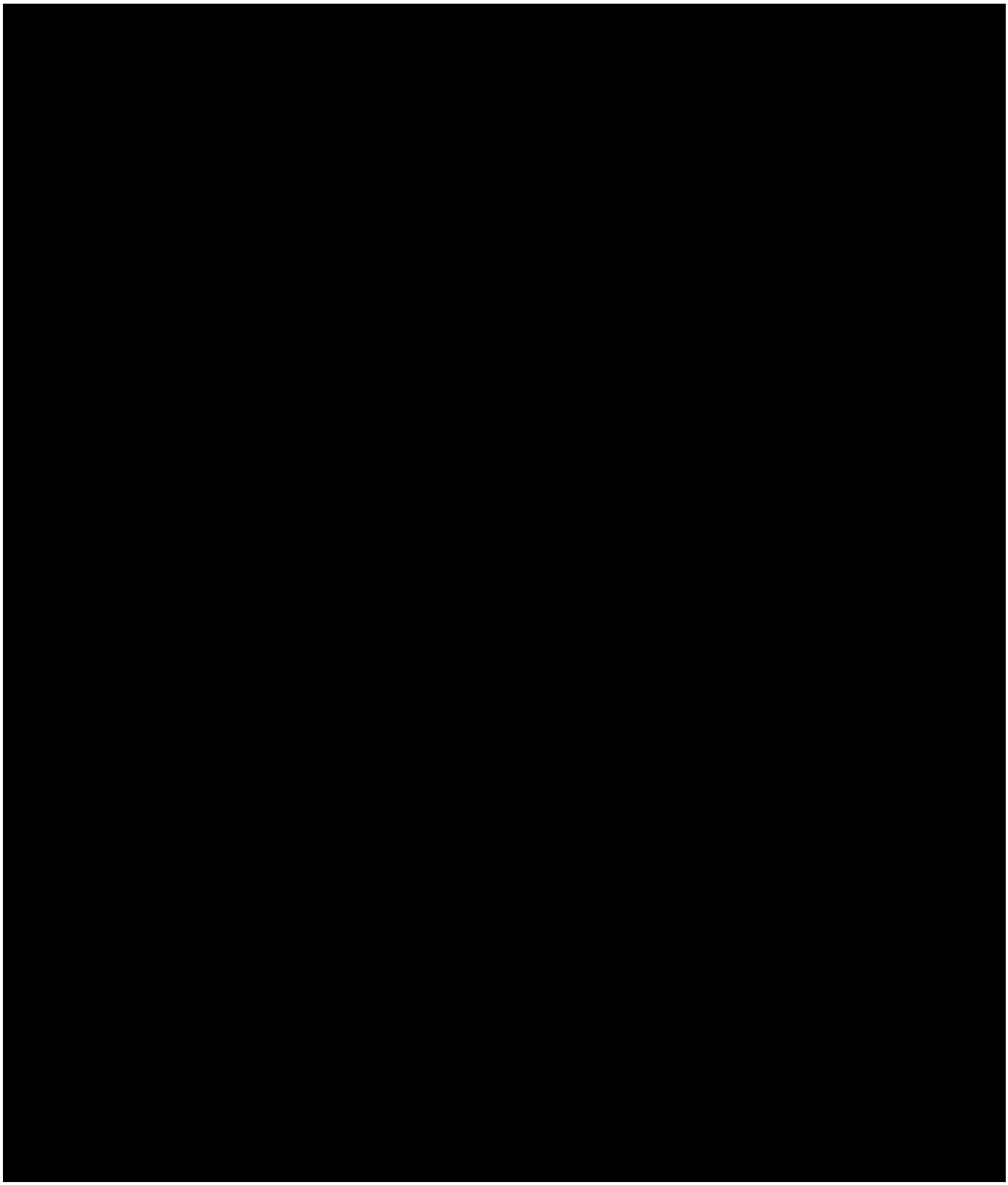

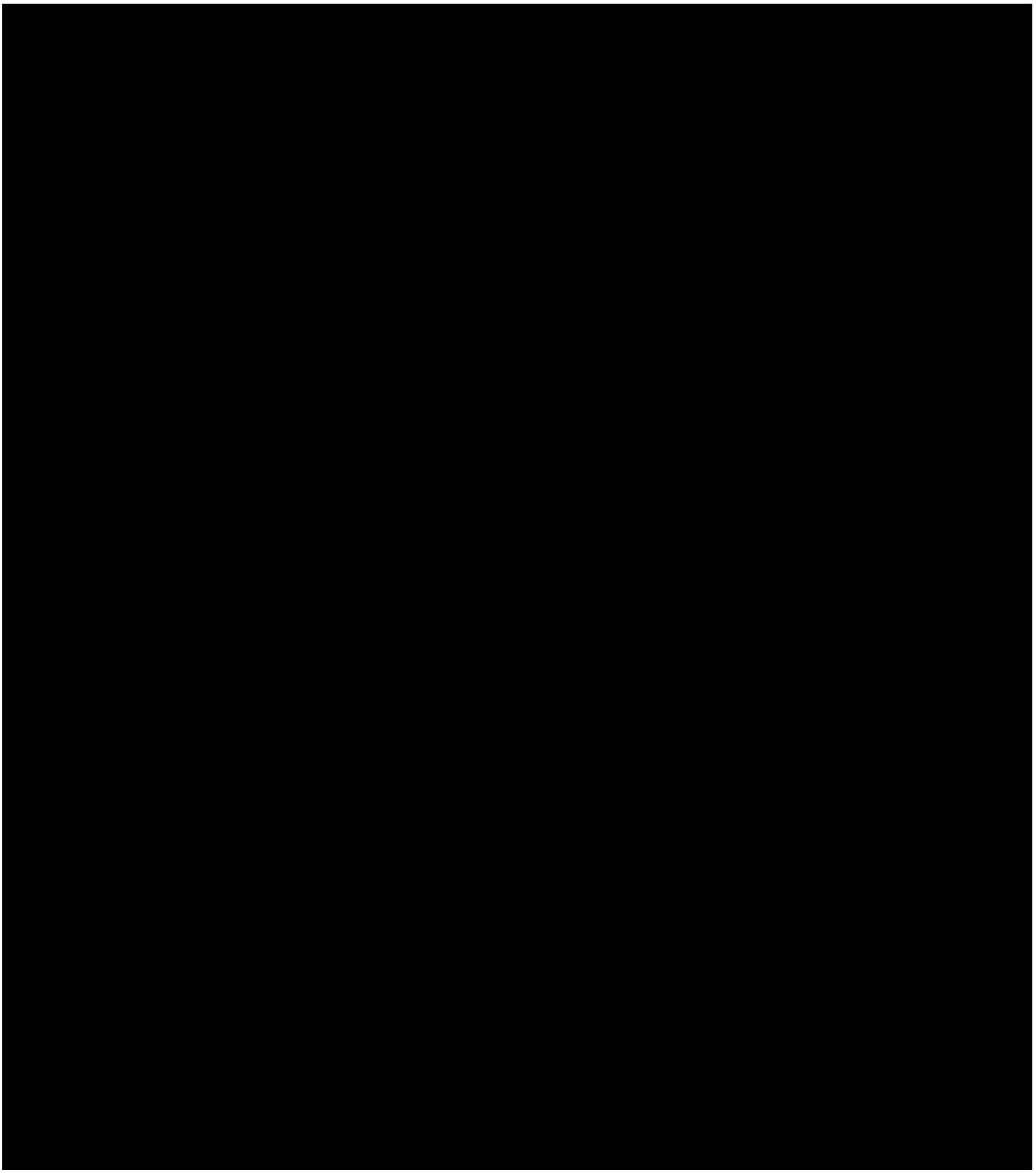

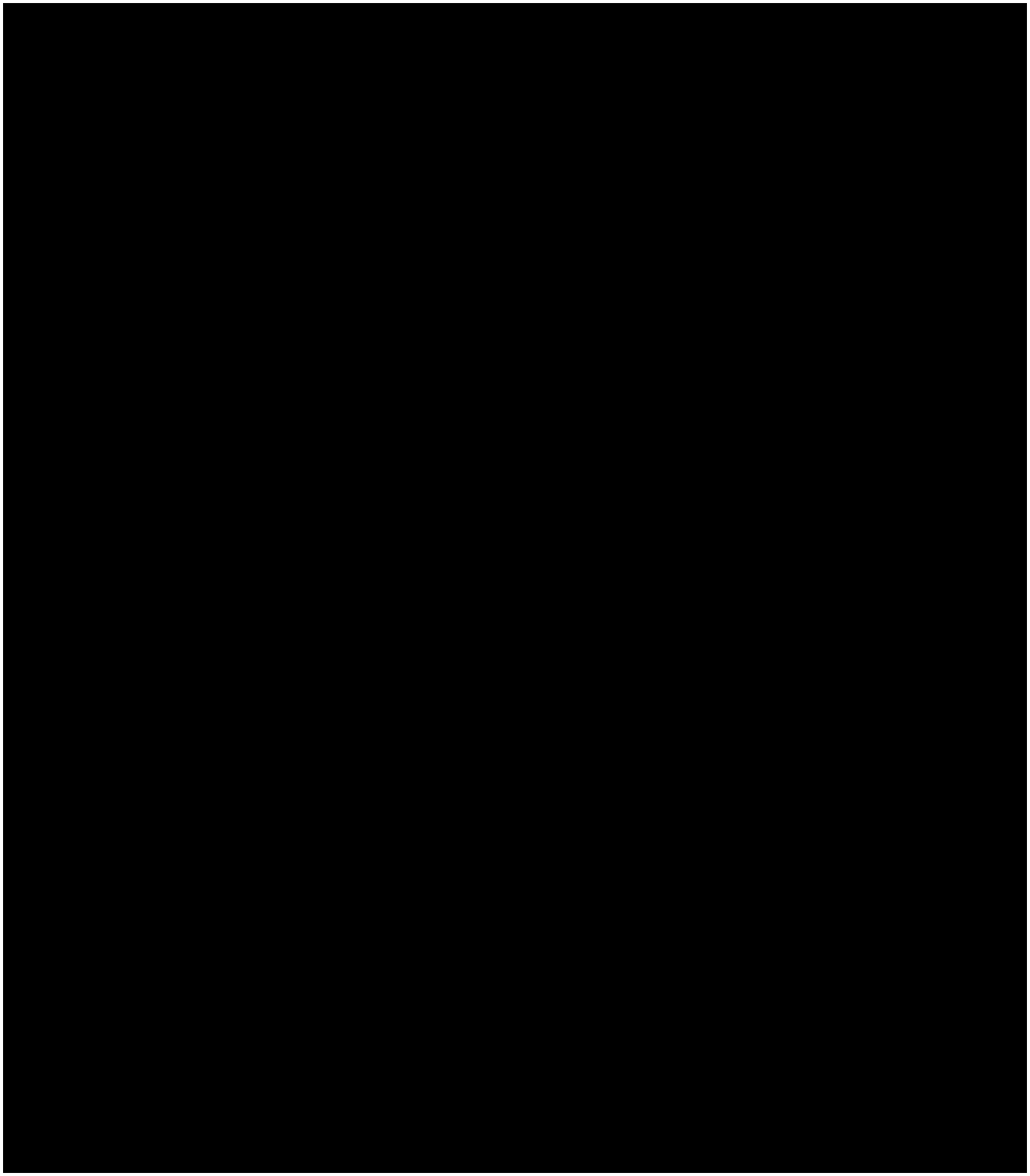

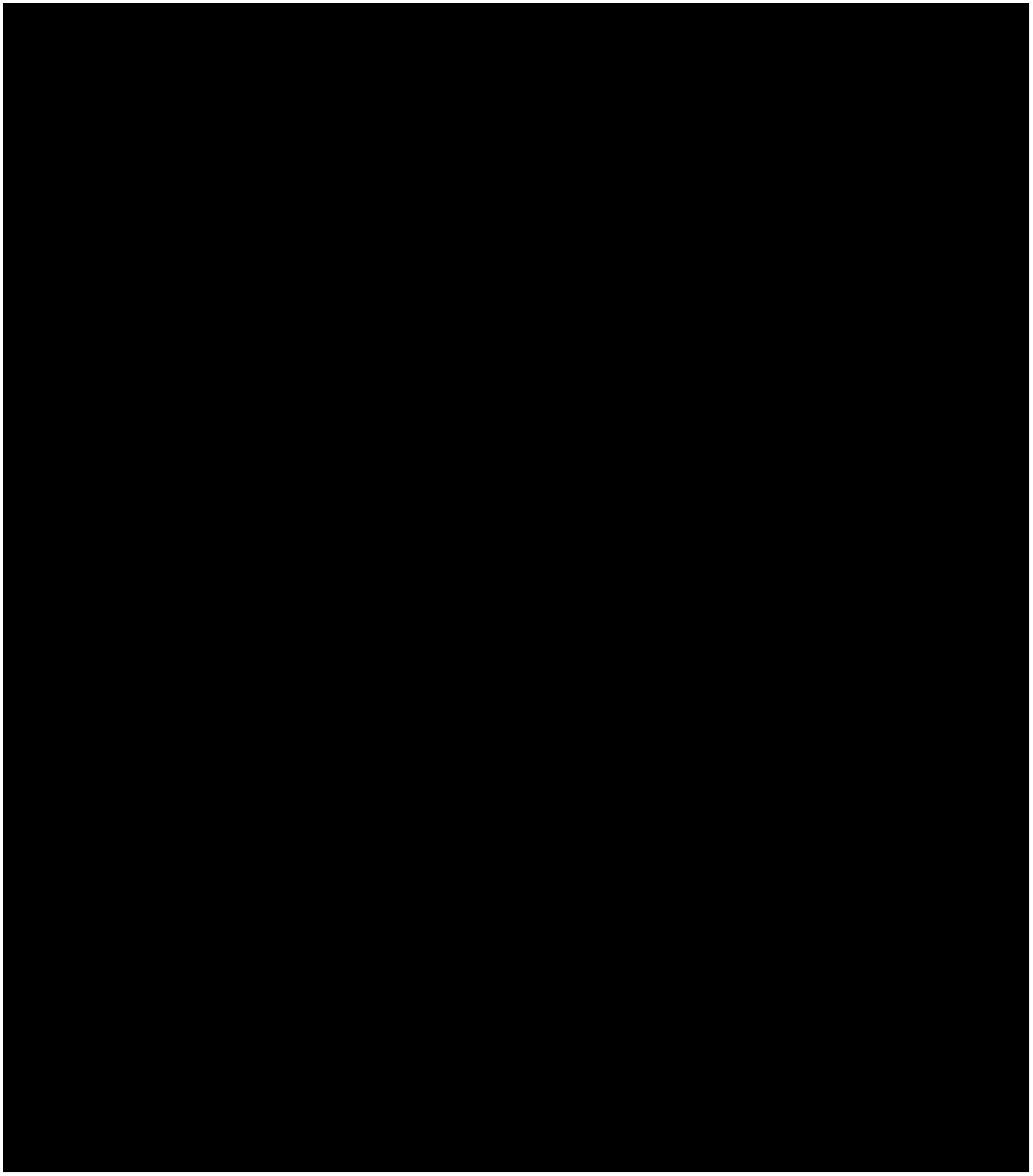

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