Hoge Gezondheidsraad

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Genetische zelftests

In this scientific policy advisory report, the Superior Health Council provides recommendations and policy options which promote an ethically and medically appropriate offer of direct-to-consumer genetic tests, such as that provided through the Belgian healthcare system

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1. INLEIDING EN VRAAGSTELLING

I. Inleiding

In het kader van dit advies worden genetische zelftests gedefinieerd als het adverteren, verkopen of (vrij) ter beschikking stellen van genetische tests rechtstreeks aan de consument. Deze definitie van genetische zelftests heeft geen betrekking op genetische tests die worden uitgevoerd in het kader van biomonitoringprojecten uitgevoerd door bonafide onderzoekers, die zijn goedgekeurd door een medisch-ethische commissie en de vereisten inzake geïnformeerde toestemming naleven. Zoals reeds door de *Human Genetics Commission* gesuggereerd, omvat dit debat ook "tests die in opdracht van de consument worden uitgevoerd", d.w.z. tests die weliswaar buiten het zorgstelsel gebeuren, maar waarvoor een arts of een gezondheidswerker betrokken is bij het aanvragen van de tests of het meedelen van de uitslag (HGC, 2010).

De afgelopen decennia is het inzicht in de genetische achtergrond van ziekten enorm toegenomen. Er zijn thans meer dan 2 500 genetische tests (http://www.ncbi.nlm.nih.gov/gtr/qa/) beschikbaar in de klinische praktijk. Dat betekent dat er ook een brede waaier aan genetische zelftests op de markt te krijgen is, gaande van zelftests voor preconceptioneel dragerschap voor monogenetische aandoeningen, zoals mucoviscidose (die een hoog risico voorspellen dat het nageslacht zal getroffen zijn indien beide ouders dragers zijn) tot genetische tests die informatie bezorgen over de vatbaarheid voor multifactoriële, complexe ziekten zoals depressie en hart- en vaatziekten. Naast het verstrekken van testresultaten, verlenen een aantal commerciële privébedrijven ook aanbevelingen voor veranderingen in levensstijl op basis van deze resultaten, zoals veranderingen in het dieet of het gebruik van voedingssupplementen. Thans worden verschillende genetische tests via het internet geadverteerd, verkocht of rechtstreeks aan de consument bezorgd. Commerciële privébedrijven bieden een brede waaier aan genetische zelftests: tests voor het dragerschap van recessieve erfelijke aandoeningen, "lifestyle"-gerelateerde genetische tests, farmacogenomische tests, niet-invasieve prenatale tests (die gebruik maken van het foetaal DNA in het bloed van de moeder), liefdesrelatietests, genomische risicoprofielen voor een groot aantal aandoeningen, vaderschapstests, verwantschapstests of genealogische tests.

Genetische tests moeten om verschillende redenen zorgvuldig worden overwogen. Vanuit een maatschappelijk perspectief is bezorgdheid geuit dat genetische tests zouden kunnen leiden tot

misbruik van de aldus verkregen genetische informatie door derden, waaronder verzekeraars, werkgevers, adoptiebureaus of anderen, en/of zouden kunnen leiden tot de stigmatisering of discriminatie van individuen of groepen. Bovendien zijn er vraagtekens geplaatst bij het persoonlijke en vertrouwelijke karakter van genetische informatie. Op een persoonlijk niveau zou de uitslag van de genetische test van een persoon rechtstreekse gevolgen kunnen hebben voor zijn/haar familieleden, met inbegrip van het nageslacht. Voorts zouden genetische tests informatie kunnen leveren over de medische toekomst van een gezonde persoon, wat globaal verschillend is van de traditionele medische diagnose, die iets zegt over de huidige medische toestand van een patiënt. Tot slot is gemeld dat een genetische test ook kan leiden tot psychische nood, met inbegrip van toegenomen angstgevoelens, depressie, vertroebelde familiale betrekkingen, een aangetast zelfbeeld of een gewijzigde gezondheidsperceptie.

Om deze redenen worden genetische tests in de meeste Europese landen in een klinisch genetisch centrum of in andere instellingen uitgevoerd die zijn erkend en/of gecertificeerd door het nationale zorgstelsel en waar de nodige nadruk wordt gelegd op het gepersonaliseerde medische toezicht op de patiënten, pre-test en post-test counseling, psychologische follow-up en kwaliteitsborging voor de uitgevoerde tests, zoals voorgesteld door het Europees Verdrag inzake de Rechten van de Mens en de Biogeneeskunde (1997) en het Aanvullend Protocol inzake genetische tests, alsmede de aanbeveling van de Raad van Europa (CM/Rec(2010)11) over de invloed van de genetica op de organisatie van de gezondheidszorg en de opleiding van de gezondheidswerkers.

In tegenstelling tot deze praktijk, die in de gezondheidszorg de norm is, hebben in de afgelopen drie jaar commerciële privébedrijven genetische zelftests geadverteerd en verkocht (Hunter et al., 2008). *Nature* meldde dat "beschikbare en betaalbare genetische zelftests als paddenstoelen uit de grond zijn geschoten" ("*the availability of affordable, direct-to-consumer genetic tests has mushroomed*")(Nature, 2009).

Het aanbod aan genetische zelftests doet verschillende vragen rijzen over de reële of potentiële gevaren, met inbegrip van (1) het gebrek aan analytische en klinische validiteit en klinisch nut van de verkochte tests; (2) het gebrek aan kwaliteitscontrole van de tests en laboratoria die ze ter beschikking stellen, evenals de kwalificaties van het betrokken personeel; (3) de (misleidende of oneerlijke) reclame voor genetische tests; (4) het gebrekkige proces van geïnformeerde toestemming en erfelijkheidsadvisering; (5) het onethisch uitvoeren van genetische tests bij kinderen; (6) het gebrek aan gepersonaliseerd medisch toezicht; (7) de stroomafwaartse impact op het zorgstelsel en (8) de mogelijke schending van de richtsnoeren voor ethisch onderzoek.

Om deze redenen heeft de Hoge Gezondheidsraad (HGR) beslist om zich te buigen over het huidige aanbod aan genetische zelftests en de bedenkingen rond dit aanbod. Hij verstrekt aanbevelingen en suggereert beleidsopties voor een ethisch en medisch verantwoord aanbod aan genetische tests in België, zoals het huidige aanbod binnen het Belgische zorgstelsel.

Om aanbevelingen te formuleren, werd een *ad hoc*-werkgroep opgericht met experts op de volgende gebieden: geneeskunde, genetica, wetgeving inzake *in-vitro*diagnostiek, toxicologie, medische bio-ethiek, medisch recht, epidemiologie, radiobiologie, farmacogenomica.

2. AANBEVELINGEN

Aanbeveling 1: Informatie verstrekken aan gezondheidswerkers en het grote publiek

Gezien het groeiende aantal bedrijven die genetische zelftests adverteren en verkopen, is de HGR van oordeel dat het essentieel is om aan gezondheidswerkers en het grote publiek achtergrondinformatie te verstrekken over genetische tests, alsook om de dienstverlening op dat vlak te beschrijven. Aan de ene kant is het belangrijk te benadrukken dat er klinisch gevalideerde en medisch geschikte tests in klinische structuren beschikbaar zijn voor wie ze nodig heeft en dat deze door de gezondheidszorg terugbetaald worden. Het is echter ook belangrijk om de beperkingen van de tests, die op het internet geadverteerd, aangeboden en verkocht worden alsook de bezorgdheid die ze doen rijzen, toe te lichten.

Deze informatie moet beschikbaar zijn in het Engels, Frans, Nederlands en Duits op de website van de Belgische FOD Volksgezondheid en indien mogelijk ook op andere relevante websites. Bovendien moeten ook (elektronische) folders worden opgesteld en uitgedeeld aan diverse gezondheidswerkers en het grote publiek. Goede voorbeelden voor dergelijke documenten zijn deze die zijn opgesteld door de *Federal Trade Commission* in de V.S. (Federal Trade Commission, 2006) en een patiëntenorganisatie in het Verenigd Koninkrijk (Genetics Interest Group, 2009). De Raad van Europa is momenteel ook een informatiefolder over genetische tests aan het voorbereiden waarin genetische zelftests worden aangekaart. De HGR is bereid om bij de redactie et het verdelen van dergelijke informatiefolders samen te werken.

Aanbeveling 2: De huidige wetgeving dekt de genetische zelftests niet volledig

In vergelijking met landen als Duitsland, Zwitserland, Portugal en Frankrijk, heeft België geen specifiek wettelijk kader voor het aanbieden van genetische tests. Het koninklijk besluit van 14 december 1987 (gepubliceerd in het Belgisch Staatsblad van 25 december 1987) legt de regels vast voor de levering van genetische tests in de centra voor menselijke erfelijkheid in België. Voorts worden in het koninklijk besluit van 7 juni 2007 tot wijziging van het koninklijk besluit van 14 september 1984 de vereisten vastgelegd voor laboratoria die terugbetaalde moleculairbiologische tests uitvoeren waarmee verworven aandoeningen in het menselijk erfelijk materiaal worden geïdentificeerd. In België bestaat er ook een wetgeving inzake genetica en verzekeringen. In Artikel 61 van de wet op de verzekeringsovereenkomsten wordt een totaal verbod gelegd op het gebruik van genetisch onderzoek om de toekomstige gezondheidstoestand van de kandidaat-(levens)verzekerde te bepalen. Bovendien beschrijft de Wet betreffende de rechten de patiënt van 22 augustus 2002 de rechten en plichten van artsen en patiënten. Tot slot bestaat er in Vlaanderen een wetgeving inzake bevolkingsonderzoek. Hoewel in Nederland het aanbod aan dergelijke tests dankzij een soortgelijke wetgeving gedeeltelijk kan worden gecontroleerd, vallen genetische zelftests momenteel buiten de bevoegdheid van de Vlaamse wetgeving. De enige wettelijke grondslag die van toepassing is op genetische zelftests zou kunnen worden gevonden in artikel 2 van de Wet op de uitoefening van de gezondheidszorgberoepen (koninklijk besluit nr. ° 78 (Belgisch Staatsblad 14.11.1967)) [1], dat bepaalt dat een arts (erkend door het Belgische zorgstelsel) dient te worden betrokken bij het verstrekken van medische diensten waarvoor een activiteit nodig is die wordt beschouwd als de uitoefening van de geneeskunde. Hieruit volgt dat, indien genetische zelftests onder de uitoefening van de geneeskunde vallen, een arts die is erkend door het Belgische zorgstelsel

[1] Artikel 2: **[**Koninklijk besluit nr. 78 betreffende de uitoefening van de gezondheidszorgberoepen] "Niemand mag de geneeskunde uitoefenen die niet het wettelijk diploma bezit van doctor in de genees-, heel- en verloskunde, dat werd behaald in overeenstemming met de wetgeving op het toekennen van de academische graden en het programma van de universitaire examens, of die niet wettelijk ervan vrijgesteld is, en die bovendien de voorwaarden gesteld bij artikel 7, (...) niet vervult."

daarbij moet worden betrokken en dat de Wet betreffende de rechten de patiënt van toepassing is.

De meeste zelftest-bedrijven schrijven echter in hun "dienstvoorwaarden" dat ze geen geneeskunde uitoefenen, en dat de uitslagen van deze tests niet mogen worden beschouwd medische informatie, maar enkel "ter informatie" worden aangeboden. De HGR is van oordeel dat genetische zelftest-bedrijven deze beweringen maken om aan de reglementaire controle te ontsnappen. Volgens de Raad moeten het merendeel van de tests die worden geleverd door genetische zelftest-bedrijven als medische informatie worden beschouwd, wat betekent dat het hier wel degelijk gaat om de uitoefening van de geneeskunde.

De huidige regelgeving in België volstaat niet om het eventuele aanbod aan genetische tests buiten het kader van het Centrum voor Menselijke Erfelijkheid te controleren. Dat betekent dat verdere maatregelen nodig zijn. Volgens de HGR is een mogelijke optie het nagaan in hoeverre de Vlaamse wetgeving inzake bevolkingsonderzoek van toepassing is op zelftest-bedrijven die in of vanuit Vlaanderen opereren. De HGR onderstreept echter ook dat een dergelijke beoordeling zinloos is als ze maar in één enkel gewest wordt uitgevoerd. Een soortgelijke evaluatie (op basis van dezelfde criteria) moet in alle gewesten worden gerealiseerd.

Aanbeveling 3: Het internationaal toezicht verstrengen

In Europa is de regelgeving inzake medische hulpmiddelen in drie Europese richtlijnen vervat, waaronder de derde de medische hulpmiddelen voor *in-vitro*diagnostiek betreft (IVD). Deze voorziet in een regelgevend kader voor alle IVD's die binnen de EER-lidstaten, Turkije en Zwitserland op de markt zullen worden gebracht. Deze richtlijn, die in 1998 werd gepubliceerd en sinds 2003 van kracht is, bepaalt de veiligheid en de werkzaamheid van de hulpmiddelen door essentiële eisen te stellen waaraan voldaan moet worden, vooraleer een product in de handel te brengen (bv. etikettering, analytische en diagnostische werking) en met name de plicht tot postmarketing toezicht.

Genetische tests met een medisch doel vallen onder de regelgeving voor medische hulpmiddelen voor *in-vitro*diagnostiek. Thans zouden genetische tests bij mensen echter over het algemeen niet onder bijlage II (die bepaalt voor welke tests een premarketing evaluatie nodig is) vallen, en dus niet onderworpen zijn aan een overeenstemmingsbeoordeling door een onafhankelijke derde. Dit regelgevend kader zal naar verwachting worden gewijzigd (met het invoeren van een risico-model op basis van vier categorieën, variërend van hoog tot laag risico) en genetische tests zullen zeer waarschijnlijk worden verplaatst naar een risicocategorie die een premarketing evaluatie vereist.

De Hoge Gezondheidsraad wenst echter te benadrukken dat een dergelijke premarketing evaluatie de veiligheid en de werkzaamheid van het hulpmiddel het licht van de beweringen van de fabrikant onderzoekt. Het omvat geen beoordeling van het klinisch nut van het hulpmiddel. Het verdient daarom aanbeveling om essentiële eisen voor de validatie van het klinisch nut van genetische tests in de herziene IVD-wetgeving op te nemen. Er moet worden erkend dat de IVD-richtlijn geen beoordeling zal geven van de vraag of het aanbieden van een test aan de bevolking al dan geen goede medische praktijkvoering is. Ook moet worden opgemerkt dat IVD-richtlijn 98/79 /EG geen betrekking heeft op genetische zelftests die niet zijn bedoeld voor medische doeleinden, zoals tests die informatie verstrekken voor een betere levensstijl of vaderschapstests. Ook reagentia die worden geproduceerd binnen de laboratoria van instellingen voor gezondheidszorg om in die omgeving te worden gebruikt en die niet zijn onderworpen aan handelstransacties, vallen niet onder de IVD-richtlijn 98/79/EG. Tot slot moeten de belangrijkste tekortkomingen van de richtlijn voor medische hulpmiddelen voor *in-vitro*diagnostiek in verband met genetische zelftests op internationaal niveau worden aangepakt.

Aanbeveling 4: Nationaal toezicht uitvoeren

Gezien de lacunes in de toepasbare wetgevingen, pleit de HGR voor het uitwerken van een regelgevend kader voor het aanbieden van genetische tests in alle mogelijke contexten in België. Hoewel het onmogelijk is om een internationale markt van genetische tests die via het internet worden verkocht of geadverteerd, te controleren of te beperken, adviseert de HGR om wettelijke belemmeringen op te werpen voor bedrijven die genetische tests voor de Belgische markt zouden aanbieden of adverteren. De gevolgen voor de volksgezondheid worden immers des te aanzienlijker wanneer bedrijven deze tests in de taal van het land en van de gebruiker op de markt brengen en verkopen, wat regelgevende maatregelen rechtvaardigt.

In het licht van de internationale inspanningen van de Raad van Europa, pleit de HGR voor de omzetting in nationale wetgeving van de inhoud van het "Aanvullend Protocol bij het Verdrag inzake de Rechten van de Mens en de Biogeneeskunde inzake Genetische Tests voor Medische Doeleinden". Bepaalde artikelen van dit Aanvullend Protocol leggen het accent op informatievoorziening, erfelijkheidsadvisering, de toestemmingsprocedure en het recht op privacy.

Bovendien adviseert de HGR om de wetgeving die in andere landen is uitgewerkt, te gebruiken als uitgangspunt voor de Belgische wetgeving. Hier is de Zwitserse wetgeving (Federale wet inzake genetisch onderzoek bij de mens, *Bundesgesetz über genetische Untersuchungen beim Menschen* (Bondsvergadering van de Zwitserse Confederatie, 2004) van 8 oktober 2004 (Sprumont, 2004) van bijzonder belang. In deze wet wordt immers een kader opgericht dat tot doel heeft om een verkeerd gebruik van genetische tests en genetische gegevens te voorkomen en om de kwaliteit van genetische tests en de manier waarop hun resultaten worden geïnterpreteerd, te waarborgen. Er worden algemene beginselen beschreven zoals niet-discriminatie, toestemming, het recht om niet te weten, de bescherming van de genetische gegevens, de toelating om genetische tests uit te voeren. Ze bevat ook specifieke artikels over het gebruik van genetische tests in een medische context, in het kader van arbeidsverhoudingen, verzekeringen, aansprakelijkheid en afstamming. De genetische zelftests beantwoorden aan de definitie van "medische hulpmiddelen voor *in-vitro*diagnostiek", zoals geformuleerd in artikel 3j van de bovengenoemde wet: "Gebruiksklare producten om eigenschappen van menselijk erfelijk materiaal te bepalen" (*Genetische In-vitro-Diagnostika: verwendungsfertige Erzeugnisse zum Nachweis von Eigenschaften des Erbguts*). Deze tests vallen onder artikel 9 van deze wet, dat het volgende bepaalt: “(1) Het is verboden om medische hulpmiddelen voor *in-vitro*diagnostiek aan individuen te leveren voor een gebruik dat niet kan worden toegeschreven aan hun professionele of commerciële activiteiten; (2) De Bondsraad kan voorzien in uitzonderingen op dit verbod na overleg met de Expertencommissie voor genetische tests bij mensen, op voorwaarde dat de producten worden gebruikt onder medisch toezicht en geen verkeerde interpretatie van het testresultaat mogelijk is". *((1) Es ist verboten, genetische In-vitro-Diagnostika an Personen für eine Verwendung abzugeben, die nicht der beruflichen oder gewerblichen Tätigkeit dieser Personen zugerechnet werden kann.(2) Der Bundesrat kann, nach Anhörung der Expertenkommission für genetische Untersuchungen beim Menschen, Ausnahmen von diesem Verbot vorsehen, sofern die Verwendung unter ärztlicher Aufsicht erfolgt und keine Fehlinterpretation des Untersuchungsergebnisses möglich ist.).* Deze wet is aangevuld met twee ordonnanties: de ordonnantie van de Bondsraad over genetische tests bij mensen van 14 februari 2007 (Bondsvergadering van de Zwitserse Confederatie, 2007) en de ordonnantie van het Federaal Departement van Binnenlandse Zaken inzake genetische tests bij mensen van 14 februari 2007(Federaal Departement van Binnenlandse Zaken, 2011). In deze reglementering is nergens een uitzondering voorzien op artikel 9 van de wet, die genetische zelftests verbiedt. Volgens de wet (Sprumont, 2004) is het zelfs een misdrijf om dit verbod schenden, zoals bepaald in artikel 38: “(1) Wie in strijd met artikel 9, paragraaf 1, opzettelijk medische hulpmiddelen voor *in-vitro*diagnostiek aan personen levert voor een gebruik dat niet kan worden toegeschreven aan de professionele of commerciële activiteiten van deze personen, wordt gestraft met een boete; (2) Wie deze feiten voor commerciële doeleinden pleegt, wordt veroordeelt tot een

gevangenisstraf van maximaal drie jaar of een geldboete." (*Wer vorsätzlich entgegen Artikel 9 Absatz 1 genetische In-vitro-Diagnostika an Personen für eine Verwendung abgibt, die nicht der beruflichen oder gewerblichen Tätigkeit dieser Personen zugerechnet werden kann, wird mit Busse bestraft. (2) Wird die Tat gewerbsmäßig begangen, so ist die Strafe Freiheitsstrafe bis zu drei Jahren oder Geldstrafe*)

De HGR adviseert dat België een wetgeving toepast die vergelijkbaar is met de wetgeving die in Zwitserland werd opgericht met betrekking tot genetische zelftests voor gezondheidsdoeleinden. Aan de ene kant legt deze wetgeving een duidelijk verbod op het aanbieden van genetische zelftests, terwijl ze aan de andere kant voorziet in een procedure voor bedrijven die dat zouden willen doen, en vereist dat deze tests onder medisch toezicht worden geleverd, dat ze een aangetoond, gevalideerd en gepubliceerd klinisch nut hebben en dat de rechten van de patiënt worden gegarandeerd. Ze vereist ook dat de patiënt correcte informatie krijgt. Zoals het geval is in Zwitserland, moet een Belgische interdisciplinaire federale commissie (die bestaat uit experts in zowel klinische, humane alsook public health genomics, farmacologie, beoordeling van gezondheidstechnologie, volksgezondheid, rechten, ethiek) worden belast met het toezicht op en de evaluatie van de genetische zelftests die op de Belgische markt worden aangeboden, alsook met de taak ervoor te zorgen dat bedrijven die deze test leveren, de gestelde vereisten naleven.

Aanbeveling 5: Het aanbod reguleren, niet het gebruik

De HGR wijst erop dat bij het opleggen van beperkingen (zie aanbeveling 4) de nadruk moet liggen op de bedrijven die genetische tests adverteren en verkopen. De personen die voor zichzelf genetische tests bestellen, zouden niet beboet of gecriminaliseerd mogen worden. Het vragen van een genetische test op materiaal van een derde persoon, zoals een minderjarige, moet echter wettelijk worden bestraft als dit niet wordt gedaan door een erkende arts. Ook de Zwitserse wet voorziet niet in uitdrukkelijke sancties tegen een persoon die een dergelijke test aanvraagt voor eigen gebruik.

Aanbeveling 6: Bijkomende studies en debat zijn nodig

Ten eerste benadrukt de HGR dat hij niet de eigenschappen heeft onderzocht van zelftests voor niet-invasieve prenatale diagnose. De mogelijkheid om het geslacht van de baby in het begin van de zwangerschap te bepalen, zou bijvoorbeeld kunnen leiden tot een stijgende vraag naar abortussen om niet-medische redenen binnen de door de huidige wetgeving voor abortus toegestane termijn, wat zware gevolgen zou hebben voor ons zorgstelsel. Over dit onderwerp is meer interdisciplinair overleg nodig.

Voorts onderstreept de HGR dat het aanbod van zelftests voor preconceptioneel dragerschap de preconceptiezorg in vraag stelt en ook het systematisch aanbieden van dragerschapstests aan paren met een kinderwens. Een dergelijk systematisch screeningsaanbod bestaat momenteel niet in ons zorgstelsel. Het zou echter nog grotere gevolgen voor ons zorgstelsel kunnen hebben. Ook hier is meer interdisciplinair overleg nodig.

Ten derde wijst de HGR erop dat verschillende zelftest-bedrijven verwantschapstests of genealogische tests aanbieden. Hoewel deze tests minder problematisch van aard zijn dan het huidige aanbod van genetische zelftests, is gebleken dat zij het mogelijk maken om biologische verwanten op te sporen (zoals anonieme gametendonoren of adoptiedonoren (en hun verwanten)). Er is meer interdisciplinair overleg nodig over de toenemende problemen om de anonimiteit van gametendoren te beschermen in het kader van kunstmatige voortplantingstechnieken en de gevolgen daarvan op het vlak van adoptie.

KEYWORDS

Keywords	Mesh terms*	Sleutelwoorden	Mots clés	Stichwörter
Direct-to-consumer		Rechtstreeks voor de consument	Directement au consommateur	direkt an die Verbraucher
Genetic testing	Genetic Testing	Genetische testen	Test génétiques	Genetische tests
Biomedical ethic	Bioethics	Biomedische ethiek	Ethique biomédicale	Biomedizinische Ethik
Regulation	Legislation as Topic	Reglementering	Règlementation	Vorschriften
Healthcare system	Delivery of Healthcare	Gezondheidszorg systeem	Système de soins de santé	Gesundheitssystem

** MeSH (Medical Subject Headings) is the NLM controlled vocabulary thesaurus used for indexing articles for PubMed.*

3. FURTHER DETAILS AND ARGUMENTATION

List of abbreviations

BRCA :	Breast Cancer
CF :	Cystic Fibrosis
DNA :	Deoxyribose Nucleic Acid
DTC:	Direct to consumer
EEA :	European Economic Area
EGAPP :	Evaluation of Genomic Applications in Practice and Prevention
FDA :	Food and Drug Administration
GAO :	Government Accountability Office
GenDG :	The Genetic Diagnosis Act
GHTF:	Global Harmonisation Task Force
GT :	Genetic Test
HbP :	High Blood Pressure
HGC :	Human Genetics Commission
IVD :	In Vitro Diagnostic
LDT :	Laboratory Developed Test
PSA :	Prostate Specific Antigen
SHC :	Superior Health Council
SNP :	Single Nucleotide Polymorphisms

I. Methodology

This advisory report is based on a review of the scientific literature as well as the grey literature, and on the experts' opinion.

II. Direct-to-consumer genetic testing: the offer

1. Types of tests

It is not really possible to provide a complete overview of the genetic tests that are currently advertised or sold directly-to-consumers. However, it is clear that the active companies cover a very broad spectrum of tests, and some companies provide more than one type of test in their offer:

1) Various commercial companies currently offer DTC **carrier tests for recessive genetic disorders**. Identifying carriers of autosomal recessive or X-linked disorders before pregnancy has

the potential to benefit prospective parents. Couples can become aware of the possible genetic risks to future offspring and of the reproductive options available. These options include not only prenatal diagnosis followed (or not) by termination of the pregnancy in case of an affected fetus or coming to terms with the risk, but also deciding to refrain from having children, adopting, using donor sperm or eggs, or making use of preimplantation genetic diagnosis. In some culturally-related marriage practices, it could also result in choosing a different partner. The details of the offer provided by each company, however, vary greatly. The company *DNA Direct* (www.dnadirect.com) advertised for one individual carrier test (for CF) and one carrier testing panel (for Ashkenazi Jews). The company *DNATraits* says that they are "committed to making all medically validated tests available to consumers rapidly, inexpensively and understandably" (www.dnatraits.com/compare accessed 03/05/2010) and sells a limited number of individual tests (e.g. for Alpha-1-Antitrypsin Deficiency) as well as panels of disorders (e.g. an Ashkenazi Jewish Genetic Disease Panel or a sickle cell/beta-thalassemia panel). Along with risk assessment information on other disorders, *Pathway Genomics* (www.pathway.com) and *23andMe* (www.23andme.com) include in their full genome testing report the carrier status for 37 and 24 different single-gene conditions, respectively. In February 2010 the company *Counsyl* (www.counsyl.com) launched their offer of a prepregnancy 'universal carrier test', which tests an individual or couple for over 100, mostly autosomal recessive, genetic diseases. *Counsyl* considers these activities as " a cause, a campaign to finally end the needless suffering of preventable genetic disease" (https://www.counsyl.com/about/counsyl/ accessed 19/01/2011).

2) Several companies provide genetic testing for individual **"life-style"-related genetic traits**. In contrast with the previous category, these tests focus on particular traits or predispositions. Here are a few examples: based on studies suggesting that the ACTN3 gene has an impact on athletic performance, companies such as Atlas Sports Genetics (http://www.atlasgene.com/), Genetic Technologies (http://www.gtglabs.com/), American International Biotechnology Services (http://www.sportsxfactor.com/Home.aspx), Inneova (www.inneova.com) and CyGene Direct (http://www.cygenedirect.com/) sell tests that aim to provide "parents and coaches early information on their child's genetic predisposition for success in team or individual speed/power or endurance sports." (http://www.atlasgene.com/ Accessed 7 June 2011) Companies like Consumer Genetics (http://www.consumergenetics.com/), Gene Planet Limited (http://www.geneplanet.com/), My Gene (http://mygene.com.au/) provide genetic tests that "will tell you if you have the fast or slow caffeine metabolizing gene" (http://www.consumergenetics.com/DNA-Tests/Caffeine-Metabolism-Test.php Accessed 7 June 2011) Companies as Salugen (www.salugen.com), Amway (www.amway.com), Interleukin Genetics (http://www.ilgenetics.com/), Holistic Health International (http://www.holistichealth.com/) offer nutrigenomic tests and often combine their genetic tests with purchasing particular dietary supplements that are recommended and tailored to the individual needs of the consumers depending on the test results.

3) Various companies provide **pharmacogenomic tests**, such as genetic tests for drug response for inhalers containing beta-agonists (albuterol, solbutamol, salmeterol), Plavix, Tamoxifen or Warfarin. These tests are provided by companies such as Consumer Genetics (http://www.consumergenetics.com/), Matrix Genomics (http://www.matrixgenomics.com/), DNAdirect (www.dnadirect.com) or Genelex (http://www.healthanddna.com/).

4) Some companies offer non-invasive DNA-paternity testing or gender testing. This is for example done through companies like the Prenatal Genetics Center (http://www.prenatalgeneticscenter.com/), ACU-gen Biolabs (www.babygendermentor.com) or Urobiologics (http://www.urobiologics.com/).

5) A company like Scientific Match (www.scientificmatch.com) sells a DNA test as a complementary way of finding a romantic relationship.

6) Some companies such as 23andme (www.23andme.com), Navigenics (www.navigenics.com), deCodeMe (www.decodeme.com) or Pathway genomics (www.pathwaygenomics.com) offer "genetic profiles", which involves testing over half a million single nucleotide polymorphisms (SNPs; these are positions in the genome at which the nucleotide varies within a population), and claim to be able to provide personal information regarding many disorders. They use information from scientific studies to estimate composite risk factors for diseases based on each customer's

SNPs. The vision offered here is to convey an all inclusive test for known genetic variants associated with susceptibilities for disease or behavioral traits and abilities. They also provide information about ancestry, carrier status or pharmacogenomics.
7) Various companies provide non-medically oriented information. This includes the offer of ancestry and genealogical tests, as well as tests identifying family relationships (e.g. paternity testing). Ancestry testing is done by companies such as Family Tree DNA (www.familytreedna.com), DNA diagnostic Center (www.ancestrybydna.com) or Nimble Diagnostics (http://nimblediagnostics.eu).
8) Finally, it should also be observed that the company called Myriad launched a massive advertisement campaign a few years ago for a predictive genetic test for breast cancer (BRCA1 and BRCA2). (Matloff & Capaln, 2008;Mouchawar et al., 2005).

2. Vision promoted by DTC companies[2]

The main notions used in the marketing of DTC genetic tests are autonomy, empowerment, prevention, convenience, and privacy. One of the main aspects outlined in the vision of these companies is that individuals want to have a more active role in the creation, storage and protection of their personal genetic information. They promote the notion that avoiding the traditional encounter with a healthcare professional will result in a better guarantee of privacy, at least with respect to insurance companies and employers. Moreover, DTC genetic tests allow consumers to collect their own saliva samples (from which DNA is then extracted) from the comfort of their own home. For some tests, the companies argue that this does away with the burden of scheduling an appointment with a physician as well as appointment fees that would otherwise be billed in addition to the laboratory fees (Berg & Fryer-Edwards, 2008). Companies also allege that this model will allow for increased access to genetic technologies for all consumers. Furthermore, these companies suggest that this provides "the foundation for truly personalized medicine in which individuals are empowered not only with self-knowledge of their genetic risk, but also with the ability to take informed actions to prevent disease and preserve health"(Ledley, 2002).

3. Success and failure of the DTC market[3]

Presently, little is known about the actual number of genetic tests sold by DTC genetic testing companies. A few American studies have shown that only a relatively small percentage of the US population is aware of the availability of direct-to-consumer genetic tests and only a fraction of these have applied for such tests (Goddard et al., 2006; Goddard et al., 2006; Kolor et al., 2008). In a recent study by Wright and Gregory-Jones, the authors attempted to estimate the size of the DTC whole genome scan market using the Internet traffic on three companies' websites as a proxy for their commercial activity (Wright & Gregory-Jones, 2010). Despite the limited scope of interpretation and generalization allowed by this method, their conclusion that the demand for whole genome scans is fairly small is congruent with the previous studies. That being said, they still estimated the market for the three most prominent genome profiling companies (23andme, deCODE and Navigenics) to be around US $ 10-20 million in 2009.
An analysis of DTC genetic testing companies' activities in this field shows that various genetic tests that were marketed are no longer available for purchase from certain companies. For example, the following tests are no longer available for purchase: tests that predicted AIDS progression based on an analysis of CCR5-Delta 32 and CCR2-64I genes (www.hivgene.com, www.hivmirror.com); nutrigenomic tests (www.mycellf.com, www.genecare.co.za, www.integrativegenomics.com); risk assessment tests for various common disorders such as cardiovascular disease, osteoporosis, immune system defects, Alzheimer Disease (www.genovations.com, www.smartgenetics.com, www.qtrait.com); tests for addiction

[2] Based on Borry P, Cornel MC, Howard HC. Where are you going, where have you been. Direct-to-consumer genetic tests for health purposes. Journal of Community Genetics 2010; 1(3):101-106.
[3] Based on Borry P, Cornel MC, Howard HC. Where are you going, where have you been. Direct-to-consumer genetic tests for health purposes. Journal of Community Genetics 2010; 1(3):101-106.

(www.docblum.com); pharmacogenomic tests (www.signaturegenetics.com); carrier testing for disorders such as cystic fibrosis (www.udlgenetics.com). Meanwhile, some companies retracted their product from the market temporarily for unknown reasons (www.genotrim.com, www.psynomics.com) and it is unclear whether they will be available again. Other initiatives, such as the free "comprehensive genetic test" (www.geneview.com), have also disappeared. Since these companies have, for the most part, left the market in silence, it is difficult to understand exactly their reasons for doing so. One may suggest that the consequences of the global financial crisis (starting in 2007-2008) may have contributed to the downfall of some of these companies (i.e: failure to find enough paying customers). That being said, it seems that various companies also struggled with intellectual property rights (Bandelt et al., 2008; Knowledge Wharton, 2009) and the legal requirement that a physician should be involved in the ordering of genetic tests (Wadman, 2008) (which is the case in some states in the USA such as Connecticut and Michigan). Furthermore, companies testing only a few mutations (with each mutation corresponding to one trait) may have had difficulties competing with companies like 23andme, which offer full genome scans (Hayden, 2008). Other companies deliberately chose to focus on ancestry testing, and have avoided making statements about health risks (Altman, 2009). Such companies offering DNA tests for genealogical information now exist in abundance (Bandelt et al., 2008).

4. DTC genetic testing in the European context

It is clear that, at the moment, most DTC companies operate from the United States. However, there are reasons for concern, as these companies will try to attract more consumers from the European market. A study has revealed that, at the moment, 33% (41/123) of the European clinical geneticists have already been contacted by patients before undergoing or considering to undergo a DTC genetic test; and 45% (54/121) have been contacted by patients having undergone a DTC genetic test (European Society of Human Genetics, 2011). The companies most often mentioned were 23andme, Navigenics and deCodeme.

Moreover, the number of companies operating from Europe is slightly increasing. Although the manner in which they operate is not always clear, they all seem to advertise and/or sell genetic tests directly-to consumers. The company Gene Planet Limited (http://www.geneplanet.com/) has its headquarters in Dublin (Ireland), but operates from Slovenia. The company Genetic Health operates in the United Kingdom (http://www.genetic-health.co.uk/). The company My Gene Profile operates from the U.S. and from the U.K. (http://www.mygeneprofile.com/). A company like Medichecks (U.K.) advertises over 1,200 health checks and blood tests online. (http://www.medichecks.com). For some, a medical prescription is necessary. The company Genepartner GmbH (www.genepartner.com) operates from Switzerland. The company Genosense operates in Austria (http://www.genosense.com). In Spain, the company Progenika Biopharma (www.progenika.com) advertises some tests. A company in Portugal advertises genetic tests for common disorders, but requires a medical prescription (http://www.genetest.pt). In Belgium, the company Euramedica BVBA/Pharmagenoma Europa is also mentioned as a distributor for a genetic test advertised by the company Hair DX (www.hairdx.com). In the Netherlands, the company Geneticom announced that it would start selling DTC genetic tests, but finally gave up its plans (www.geneticom.nl). There are a few companies that operated in Europe whose websites are no longer available (www.g-nostics.com (U.K.); www.genosolutions.com (Portugal), www.udlgenetics.com (U.K.). Finally, it is also important to raise the question how commercial laboratories operate. The Belgian company Gendia (www.gendia.net), which does not advertise directly-to-consumers, was mentioned in the study (European Society of Human Genetics, 2011) by clinical geneticists as a company where patients could receive genetic tests without going through a healthcare professional.

III. Direct-to-consumer genetic testing: concerns

The offer of DTC genetic tests raises various concerns, the most important of which are the following : (1) the analytical validity, clinical validity and clinical utility of the tests being sold; (2) the quality control of the tests and laboratories involved in providing the tests as well as the

qualifications of the personnel involved; (3) the advertisement of genetic tests; (4) the process of informed consent and genetic counseling; (5) the genetic testing of children; (6) the lack of individualized medical supervision; and (7) the downstream impact on the healthcare system. A few additional concerns are raised in the conclusion to this section.

1. Analytical validity, clinical validity and clinical utility

Most of the DTC genetic tests that are currently available provide information on a susceptibility or predisposition for common disorders or traits. Huge concerns revolve around issues such the analytic validity and the clinical validity of these tests. Analytic validity refers to "the accuracy with which a particular genetic characteristic (e.g. a DNA sequence variant) can be identified in a given laboratory test" (Burke, 2002). Although there is, as of yet, no report regarding the performance of the genotyping methods within a commercial setting, most researchers consider the analytic validity of the methods used to be rather high (Hunter, 2008). Clinical validity refers to the strength of the association between the genotype and disease. Basically, if the risk-genotype is identified in an individual, what are the chances that he or she will develop the disease (Wade & Wilfond, 2006) ? Within the context of common multifactorial diseases (apart from a small number of exceptions), most genotype-disease associations are very weak. Many concerns with regard to the commercial offer of DTC genetic testing are based on the meaningless predictive value of the tests currently offered. As denoted by Janssens et al. (2008), "there is insufficient evidence to conclude that genomic profiles are useful in measuring genetic risk for common diseases or in developing personalized diet and lifestyle recommendations for disease prevention." Similar reports have described the limited value of risk prediction models which are only based on genetic information. (Mihaescu et al., 2009; Janssens & van Duijn, 2010; Janssens et al., 2011; Mihaescu et al., 2011; Palomaki et al., 2010). Likewise, in the U.S.A., the Government Accountability Office (GAO) (Kutz, 2006) investigated the legitimacy of claims made by nutrigenetics companies who advertised being able to provide personalized nutrition and lifestyle recommendations based on genetic information. The GAO concluded that "the tests we purchased [from these nutrigenetics companies] mislead the consumer by making health-related predictions that are medically unproven and so ambiguous that they do not provide meaningful information to consumers." Multifactorial disorders are hypothesized to occur due to a complex interaction of multiple genes and environmental factors; both individual and compounded factors are poorly understood. Each genetic and environmental factor often contributes only a modest fraction of the risk of developing the disorder, therefore making it extremely difficult to assign an accurate and meaningful degree of risk to each different factor.

Also in the context of the identification of autosomal recessive disorder carriers, there may be concerns with regard to clinical validity. Although it is likely that the analytical validity of the test for each mutation included in carrier panels offered by DTC genetic testing companies has been validated, the clinical validity (i.e. how consistently and accurately the test detects or predicts the intermediate or final outcomes of interest) of the panel of mutations may be far from 100%. Some homozygotes, because of low penetrance, may never develop overt disease, and/or the expression may be variable (Levenson, 2010). For example, this is the case for hereditary haemochromatosis, which is also included in the *Counsyl* test panel (www.counsyl.com). In addition, companies offering large panels of disorders may base their inclusion criteria on technical and economic aspects rather than on policy considerations, which take into account, among other things, carrier frequency, severity of the disorder and testing feasibility in a particular population. It also raises doubts about the individual disorders included in these large testing panels, and questions whether 'more is really better' (Leib et al., 2005). Moreover, the question is raised whether good information and informed decision making (see under clinical utility) is still possible when the test panel contains such a heterogeneous group of disorders, for which test sensitivity and specificity are variable.

Ultimately, the reason why we would want to undergo genetic testing at all has to do with a test's clinical utility. That is to say, once a genetic variant known to increase one's risk of developing a disease has been identified, how can this be useful in clinical practice? How can this be of any use to the patient who is trying to reduce his/her risk of developing a disease? Will this genetic information add to our knowledge of what should be done to prevent disease? At present,

physicians routinely recommend one or more of the following preventive measures for cardiovascular disease, diabetes, and obesity: do not smoke, exercise regularly, eat a nutritious and balanced diet, reduce stress, and control blood pressure. Genetic risk information is not likely to change these recommendations. Companies tend to sell genetic tests as 'knowledge'. Although there may be no evidence in support of the clinical utility of these tests, they claim that they might have a personal utility (Foster et al., 2009). This interpretation of utility is at odds with attempts by the clinical geneticists community to develop common standards of clinical utility, such as those being developed by the UK Genetic Testing Network (Gene Dossiers, http://www.ukgtn.nhs.uk/gtn/Information/Services/Gene+Dossiers), the EU funded Eurogentest network of excellence (Gene Cards, http://www.eurogentest.org/web/info/public/unit3/geneCards.xhtml) or the Evaluation of Genomic Applications in Practice and Prevention (EGAPP, http://www.egappreviews.org/). This interpretation of personal utility could also be at odds with a "population health validity and utility" as defined by e.g. a statement in its health policy.

2. Quality control and qualifications of personnel involved

As expressed by the statement of the European Society of Human Genetics, "all laboratories offering genetic testing services should implement an internal quality system and be subject to regular external quality assessment. Certification of laboratory procedures and accreditation of the tests offered is the standard for guaranteeing the quality of molecular genetic testing for health purposes. All persons involved in the provision of genetic services (i.e. medical doctors, nurses, genetic counselors, and biologists and technicians working at the laboratories) should have the appropriate qualifications and training and perform their role in accordance with professional best practices and ethical standards" (ESHG, 2010). It is unclear whether all laboratories providing DTC genetic testing fulfill these quality criteria. Concerns were for example expressed with regard to the qualifications and impartiality of genetic counselors or healthcare professionals hired by or linked to these companies.

3. Advertisements

Research on DTC advertising of prescription medicine has shown that this has created an inappropriate demand for medications (Calfee, 2007; Donohue et al., 2007; Schommer & Hansen, 2005; Hamp et al., 2006; Donohue, 2006; Bradford et al, 2006; Mahon, 2006). Moreover, it has been shown that various advertisements for drugs have been misleading. Overstating their effectiveness or minimizing the risks has led to consumers making inadequate or inappropriate changes in their medication, diet or lifestyle. In this respect, DTC advertising for genetic tests for health-related purposes entails the same risks as DTC advertising for prescription medicine. Aggressive marketing strategies and slogans for DTC genetic testing are liable to overstate the potential for predictive information of such tests and overrate its future health implications. An example of such an aggressive marketing strategy is provided by the following advertisement http://www.mygeneprofile.com/talent-test.html. It is likely that the aim is to increase test uptake. On most of the company websites, there is a huge difference between what can be seen on the company's homepage and in its terms of service. For example, deCodeme states on its homepage that "Now we have the ability to test someone's genetic risk for certain disease states and then make clinical decisions based on that genetic backdrop", whereas their service agreement and informed consent section warns that "The Genetic Scan product is for informational purposes only, is not medical advice, and is not a substitute for professional medical advice, genetic counseling, diagnosis, or treatment."(www.decodeme.com). Such examples cast doubt on the desirability of advertisements for genetic tests and, in any event, underline the need to ensure that advertisements should be accurate and not misleading, claims should be transparent and supported by current evidence, and complete and accurate information about the test limitations, risks and benefits should be provided.

4. Informed consent and genetic counseling

Informed consent implies that two requirements are met, viz. information and voluntary participation. As regards the first requirement, it is crucial that individuals receive the necessary

information about the purpose of a given test, the (reproductive) choices resulting from such a test, its reliability and limitations, its potential psychological impact and consequences for the individual and his/her relatives (McQueen, 2002). Privacy and confidentiality of the results, as well as the possible consequences of their being disclosed to third parties, such as insurance companies and employers, should also be discussed. Although most DTC companies do provide most of this information on their websites, the question is whether, while being commercially driven, the information presented is balanced enough to enable informed choices. Moreover, according to a recent study (Molster et al., 2009), many users would struggle to find and understand the important information they need to make an informed decision on these companies' websites.

The provision of genetic test results through a website certainly poses a series of problems. Various studies have for example shown the difficulties involved in educating people about carrier status results. The limited knowledge of genetics among the general population (Molster et al., 2009), and the fact that carrier tests have a test sensitivity of less than 100% (causing a residual risk to people who are not found to be carriers) make the goal of transmitting information about these tests a non-trivial matter. Studies have shown that a significant proportion of screen-negative tested participants who underwent preconceptional screening for CF or HbPs wrongly believed that they were definitely not carriers, while some carriers falsely believed that they were only likely to be carriers (Hartley et al., 1997; Honnor et al., 2000; Lakeman et al., 2008; Payne et al., 1997). An offer of DTC testing probably faces the same problems in educating people as has been demonstrated in these screening programs. Multiple studies have also demonstrated that both carriers and non-carriers may experience negative feelings, such as anxiety and stress, when participating in genetic screening, but anxiety levels often decrease after a few months (Lakeman et al., 2008; Bekker, 1994). Genetic results for common complex disorders are similarly complicated by the fact that they are probabilistic in nature, and must be interpreted in the context of family history, present health status and other environmental conditions (e.g. life style, diet, place of residence…). Consumers whose test results reveal a form of increased risk may over-estimate the risk they have of developing disease and this may cause needless stress and anxiety and unnecessary follow-up tests or treatments. Meanwhile, consumers with results that suggest a standard or lower than average risk of developing a disorder may understand this as meaning that they no longer have to worry about leading a healthy lifestyle. The lack of genetic counseling accompanying the provision of test results might be problematic in some cases. Genetic counseling is the process through which information enables individuals to make their own free decisions about testing. In this understanding, although all companies selling genetic DTC tests require some type of consent form to be signed when ordering a test, the process of informed decision-making cannot be reduced to signing a written document. Genetic counseling is a communication process, which deals with the occurrence, or risk of occurrence, of a genetic disorder in the family. The process involves an attempt by appropriately trained person(s) to help the individual or the family to understand the medical facts of the disorder and the options on how to deal with it. A conflict of interest may arise when the healthcare professionals involved in the counseling are employed by or linked to the companies selling the tests. In this case, impartial health advice might be compromised. Finally, current DTC services are organized in such a way that there is no control over the origin of the samples being analyzed. Most companies send mouth swab kits, as these are easier and more practical than having to send the client to a clinic where blood is drawn. Since the mouth swab is done in the privacy of the clients' home, there is no way of verifying the identity of the sample provider. That in turn makes it possible to test third parties, such as incompetent minors or incapacitated adults, and impossible to monitor this practice.

5. Genetic testing of children[4]

Clinical guidelines focusing on genetic testing in minors have emphasized that the best interest of the child is paramount and that perceived benefits and risks of testing must be carefully weighed when considering carrying out a genetic test on minors. As regards genetic tests for late onset disorders, testing has only been recommended when "established, effective, and important medical treatment" (German Society of Human Genetics, 1995) can be offered or when testing "provides scope for treatment which to any essential degree prevents, defers or alleviates the outbreak of disease or the consequences of the outbreak of disease" (Danish Council of Ethics, 2001). The rationale behind this option is that predictive and presymptomatic testing for adult-onset disease "should be delayed until the person is old enough to make an informed choice" (ESHG, 2001). The same notion applies to carrier testing, where it has been advanced that "For carrier status for conditions that will be important only in reproductive decision making, testing of children should be discouraged until the child is able to participate fully in the decision to be tested" (Bioethics Committee Canadian Paediatric Society, 2001).

However, when looking at the policies of DTC genetic testing companies (Borry et al; 2009; Borry et al., 2009) and having surveyed various DTC companies, the authors have found that several of these companies definitely test minors (Howard et al., 2011). As alluded to previously, in view of the major ethical considerations that surround predictive genetic testing and carrier testing in minors, one could question whether the same guidelines apply for tests that are described by companies as not being for the purpose of preventing, diagnosing or treating medical conditions. It is interesting to note that many companies offering DTC genetic testing declare that their services are not clinical services and should not be used as a basis for making medical decisions. For example, Consumer Genetics writes in its Authorization and Disclosure form that "all materials and products provided by Consumer Genetics, Inc. are provided for informational purposes only and are not by themselves intended for diagnosis or treatment of any disease or disorder." (www.consumergenetics.com). Various companies state that the predictive value of their genetic tests is insufficient as a useful basis for personalized nutritional and lifestyle recommendations. It is still possible, however, that consumers will overestimate the predictive value of the genetic tests (Gollust et al., 2002). Knowledge of an increased risk of disease may affect the relationship between parents and children, and cause the parents to feel guilty about the disorder itself and responsible for protecting the child from its impact (Lupton, 2001). Excessive attention to genetic risk information could also decrease the attention to non-genetic factors in disease development and lead to an overestimation of (non-validated) risk information (Grob, 2008). Moreover, by accepting children's samples submitted by their parents, some companies neglect some of their own positions with regard to the sensitive and private nature of genetic information. SeqWright states that "your genetic information is extremely sensitive. In fact, it may be the most sensitive information there is and as new discoveries are made, and more is learned about what your genes say about you, this information is likely to become evermore sensitive over time" (www.seqwright.com). DeCODE claimed that "the only people who should be able to see your genetic information are you and those with whom you choose to share it." (www.decodeme.com). Contrary to the latter two companies, which do provide testing in children, it was precisely because of these "ethical, privacy and informed consent considerations regarding genetic testing of minors for predisposition or carrier status of adult-onset genetic disorders" (www.navigenics.com) that Navigenics decide not to process samples or information from children who have not reached the age of majority.

The HGC supports the recommendations of the Advisory Committee on Genetic Testing's Code of Practice (1997) (Advisory Committee on Genetic Testing, 1997), which promotes the practice of not supplying DTC genetic testing services to those under the age of 16 or to those not able to make a competent decision on testing. The European Society of Human Genetics considered that

[4] Based on: Borry P, Howard HC, Senecal K, Avard D. Direct-to-consumer genome scanning services. Also for children? Nat Rev Genet 2009; 10(1):8. Borry P, Howard HC, Senecal K, Avard D. Health-related direct-to-consumer genetic testing: a review of companies' policies with regard to genetic testing in minors. Fam Cancer 2009; 9(1):51-59.Howard HC, Avard D, Borry P. Are the kids really all right? Eur J Hum Genet 2011.

DTC genetic tests should not be offered to individuals who have not reached the age of legal majority (ESHG, 2010).

6. Individualized medical supervision

Embedding genetic testing in a healthcare setting can ensure that adequate information is provided to increase informed choice, that the informed consent procedure is made more optimal and that there is a medical follow-up if necessary, as well as psychosocial counseling. The offer of genetic tests through the Internet by commercial companies is liable to disconnect these services completely from their usual embedding in a medically supervised context. The absence of medical supervision for most DTC tests may compromise or fail to promote patient health, especially in the case of carrier couples who may need intensive counseling on their reproductive choices and on the risks for family members. It is striking that companies are usually interested in selling tests, but not interested in supervising the medical follow-up. Most companies advise consumers to seek medical supervision in the established healthcare system at their own discretion. For example *Pathway Genomics*: "You should consult with a physician or other appropriate healthcare professional regarding the diagnosis, treatment and prevention of any disease or health condition." (http://www.pathway.com/more_info/terms_of_service accessed 04/05/2010) At present, some companies have changed their policies and require a medical prescription before a sample can be processed. The company also sends the results directly to the physician for interpretation, which means that,, technically, they no longer sell tests directly to consumers. The offer through physicians may eliminate some of the concerns that were raised about information provision, but does not resolve the issue about the appropriateness of the test sold.

7. Downstream impact on the healthcare system

"Apart from the false, misleading, non-substantial or even dangerous recommendations given or drawn from tests offered via the internet, one general danger is that, with low-quality direct to consumer genetic testing offers dominating the market, customers might lose confidence in the future in genetic testing overall. Another more direct effect could be that customers who use direct to consumer genetic testing and are left with complex, diffuse or meaningless information will increasingly look for counseling at a publicly funded centre for medical genetics or with their family doctor" (Hennen, 2008). In this way, DTC services challenge the organization of public healthcare systems. DTC services may prompt consumers to visit healthcare professionals after having had their risk of developing a disorder measured, which means that this could result in the overconsumption of healthcare services. A study (ESHG, 2011) showed that there is already a downstream impact on clinical geneticists, with consumers who have ordered tests that weren't validated and weren't clinically indicated nevertheless seeking counseling on their test results. Various companies that sell DTC genetic tests also don't want to be burdened with a medical follow-up. They often sell only the genetic tests and refer consumers to the healthcare system. For example, "Consumer Genetics, Inc. strongly urges you to discuss the result of this genetic test with your physician. You should not make any treatment decisions without first consulting your doctor." Or SeqWright: "This service cannot be used for medical diagnostic purposes. … Clients with concerns related to the information provided through this service as it pertains to an increased or decreased likelihood of developing a particular disease state, are encouraged to seek medical advice. (…) SNP data are not commonly interpreted by medical professionals. Therefore, SeqWright understands that your doctor may not be able to discuss your results in detail. It is important that you understand that association studies merely provide a statistical probability of a disease and do not serve to diagnose a disease state. With these thoughts in mind, SeqWright strictly maintains that the information and diagnoses provided by medical professionals take precedence over any information provided through SeqWright's Personal Genomic service."

8. Other concerns

Other concerns with regard to the activities of DTC companies include the research activities these companies conduct on submitted samples and the use of information without adequate

informed consent or monitoring by a research ethics committee (Howard et al., 2010). In addition, concerns were raised about what happens to the samples and data when a company goes bankrupt (Zawati et al., 2011).

IV. Direct-to-consumer genetic testing: various policy options

1. Introduction

With this long list of well-founded apprehensions regarding DTC genetic testing, it is no surprise that a number of professional (American College of Medicine Genetics , 2006; Hudson et al., 2007; ESHG, 2010) and governmental organizations (Gutman, 2005; Federal Trade Commission, 2006) and advisory bodies (HGC, 2003; HGC, 2007) have issued statements and reports warning consumers to be wary of the claims made by companies selling these tests.[5] The Belgian National Committee for Bioethics (Belgian National Committee for Bioethics, 2004) issued a statement on this subject in 2004. What is more startling and troubling is the lack of any concrete and clear regulatory framework or basic oversight of such services and company practices (Schmidt, 2008; Genetics and Public Policy Center, 2006). Discussions about this phenomenon regularly reveal the shortcomings of the current regulatory frameworks (Kaye, 2008). As many companies operate from the U.S.A., it will be crucial to see how this country will develop regulatory oversight in the future. After the partnership announcement between Pathway Genomics and the drugstore chain Walgreens to sell DTC genetic tests, the US Food and Drug Administration (FDA) decided to investigate the activities of DTC companies more carefully (Allison, 2010; Genetics and Public Policy Center, 2009). Between May and July 2010, the FDA sent letters to various companies telling them that they were unable to "identify any Food and Drug Administration clearance or approval number" (FDA, 2010). Moreover, in mid July 2010, the FDA held a meeting to discuss the oversight of laboratory developed tests (LDTs) (FDA, 2010). The issue of the (lack of) oversight of LDTs or "home brews" is closely related to that of DTC genetic testing since many of the tests offered by DTC genetic testing companies could be considered LDTs. Until now, the FDA has not required that most LDTs be reviewed for clinical validity (except for genetic tests that produce a result "for the purpose of diagnosing, treating, or preventing disease" (eg: breast cancer and prostate cancer) (Genetics and Public Policy Center, 2010). Immediately after this FDA meeting, the Committee on Energy and Commerce of the US House of Representatives held a public hearing on July 22, 2010 (Committee on Energy and Commerce, 2010), during which the report *Direct-to-consumer genetic tests. Misleading test results are further complicated by deceptive marketing and other questionable practices* by the US Government Accountability Office (GAO) was presented. Although no concrete regulatory changes have occurred since these events, it is to be expected that the FDA will take action in the future.

In order to prepare for the event of DTC companies increasingly operating in European countries, and in Belgium in particular, in the future, it is important that the Belgian health authorities take the problems related to DTC genetic testing seriously and consider various policy options. The following sections describe several fields in which actions might be necessary at the European, Belgian and regional level.

[5] For an overview see http://www.dtcgenetest.org/

2. Revision of the European Directive on in vitro diagnostic medical devices[6]

In Europe, the regulations on medical devices are set by three E.U. Directives, the third of which is the Directive on In Vitro Diagnostic Medical Devices (IVD), which provides a regulatory framework for all IVDs that are to be placed on the market within the EEA Member States, Switzerland and Turkey. This Directive, which was published in 1998 and came into force in 2003, governs the safety, quality and performance of devices by setting out the essential requirements that have to be addressed before placing a product on the market (e.g. labeling, analytical and diagnostic performances), and, among others, the mandatory post-marketing surveillance.

Although generally less burdensome than the regimes for pharmaceutical products, these legislations share a number of key features: they are concerned with ensuring the safety and performance of healthcare products. Regulating authorities have the possibility to remove existing products from the market should serious problems arise.

Genetic tests with a medical purpose fall under the regulation of in vitro diagnostic medical devices. It should be noted, however, that reagents which are produced within health-institution laboratories for use in that environment and are not subject to commercial transactions are not covered by the Directive for In Vitro Diagnostic Medical Devices (IVD).

Before placing a device on the market, the manufacturer must ensure that it meets the requirements of the Directive. Manufacturers must prepare sufficient technical documentation to demonstrate the conformity of their product, and the premarket review of this technical file is a process known as conformity assessment. Conformity assessment procedures vary depending on the risks posed by the device. Annex II to the Directive provides a list of a small number of tests which are classified as high (list A) and moderate risk (list B). Only devices listed in Annex II and devices intended for self-testing are subject to a conformity assessment by a third party, viz. a Notified Body. This pre-market review is one way of ensuring truth-in-labelling, i.e. that the manufacturer's intended use for the product is supported by the clinical data on the test's performance as set out in the technical file, and summarized in the product label and in promotional material. Human genetic testing would generally not fall within Annex II, and would therefore not be subject to a third party conformity assessment.

The Directive sets out three criteria on the basis of which tests are to be added to Annex II: "(i) whether total reliance has to be placed on the result obtained with a given device, this result having a direct impact on subsequent medical action, and (ii) whether action taken on the basis of an incorrect result obtained using a given device could prove to be hazardous to the patient, to a third party or to the public, in particular as a consequence of false positive or false negative results, and (iii) whether the involvement of a notified body would be conducive to establishing the conformity of the device." But whilst there is a set of criteria, there appears to be little consistency in what is currently classified as moderate-risk and what is looked upon as low-risk. Thus, Chlamydia tests are listed in Annex II, List B, but no other tests for sexually transmitted diseases are; PSA is also on List B, but no other cancer test is; there is one hereditary disorder, PKU, but no others. Furthermore, experience has shown that a list-based approach to classification is not an effective or future-proof risk classification mechanism for devices based on novel technologies. Due to the specific wording of Annex II, novel devices may not be subject to the

[6] Based on: ESHG - European Society of Human Genetics. Official response of the European Society of Human Genetics to the Public consultation on the revision of Directive 98/79/ec of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices 2010. Internet: https://www.eshg.org/fileadmin/www.eshg.org/documents/ESHG/ESHG-IVD-def.pdf

Eurogentest. Official response of the EuroGentest Network of Excellence in Genetic Testing to the Public consultation on the revision of Directive 98/79/ec of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices 2010. Internet: https://www.eshg.org/fileadmin/www.eshg.org/documents/received/EuroGentestResponseToIVDDRevisionConsultation.pdf

requirements laid down for high-risk devices,, which results in inconsistency. For instance, Gen-Probe's PCA3 test quantifies the PCA3 mRNA in a patient's urine sample as a marker for prostate cancer, thus performing exactly the same clinical function as the PSA test, yet it is not included in Annex II, List B.

In 2008, the European Commission held a public consultation concerning a recast of the medical devices directives. This was complemented by a public consultation held in 2010 focused on the technical aspects of the revision of the In Vitro Diagnostics Medical Devices Directive. The answers provided in the context of this public consultation confirmed the quasi unanimous support in favour of adopting a risk-based classification grounded on the Global Harmonisation Task Force (GHTF) Model. Such a risk-based classification would have a positive impact in terms of flexibility, enhancing public health protection whilst enabling a timely access to the market for new tests. In addition, the regulatory framework would become more robust to the technological progress. The GHTF model is a four-class system ranging from high- to low-risk depending on the potential impact on public health and/or the individual patient. The GHTF model places all genetic tests into the Class C category, requiring a third party conformity assessment.

There is an increasing availability of tests predicting susceptibility to common diseases such as stroke and diabetes. For the most part, such tests predict relatively minor modifications of an individual's risk and some believe that such susceptibility tests should *not* be treated with as strict regulatory scrutiny as genetic tests which provide information with much greater clinical impact, such as diagnosis of Huntington Disease or Cystic Fibrosis. However, risk classification is based on the *probability* as well as the *severity* of harm (see GHTF definitions, section 4), and there is good reason to consider that the probability of harm is greater with this class of tests, largely because of the continued uncertainty of the science, the highly polygenic nature of most common diseases, the fact that no more than a small portion of what is estimated to be the hereditary component of common diseases has been discovered to date and the speed with which genetic discoveries are being placed on the market (often as direct-to-consumer tests). Moreover, there is in some cases the possibility of severe harm. For instance, there is anecdotal evidence of people considering prophylactic surgery in the wake of being told they are at increased risk of cancer, even when the increased risk is relatively minor (Stein, 2010). As a result, it seems reasonable to require susceptibility tests to be subject to pre-market review of the sort applied to tests at a class C level.

Ambiguous risk classifications may offer manufacturers significant scope for constructing the intended uses creatively and pave the way for discrepancies between the stated intended use and the use promoted in practice (for instance, in the USA the PSA test was approved for monitoring patients diagnosed with prostate cancer but promoted for screening use). With regard to the classification of cancer testing according to the GHTF model, devices intended for cancer diagnosis would be classified in Class C, whereas screening tests would fall under Class B. Such a distinction may make sense in principle but may be difficult to implement in practice, and may lead to intentional down-classification of the device by the manufacturer. Regulatory strategies and a rigorous surveillance of post-market activity would have to be set up to deal with this and would include requiring manufacturers to include prominent warnings about the lack of data/approval for off-label uses on their label/instructions or requiring them to provide evidence on the most common clinical applications. With regard to personalized medicine, assays intended for selective therapy and management would fall within Class C, unless the clinical decision should take account of further investigation of clinical signs and symptoms. Then a down-classification to Class B is possible. The danger remains that the user, and in case of DTC genetic tests, the lay person, would not be able to identify the subtle distinctions in the instructions for use. It is preferable to clearly describe and limit/restrict the devices that fall under Class C. With regard to personalized medicine the revised legislation should clearly define what is understood by 'companion diagnostic'. With regard to the classification of devices intended to be used in screening for or in diagnosing cancer, classification of both types of devices in Class C is recommended. Furthermore, there are some categories of tests in development which might raise concern but are not discussed within the GHTF model. For instance, there is a great deal of interest in using new genomic/proteomic biomarkers for early identification of Alzheimer's disease. Such applications are fraught with potential dangers, in part because of the well-

established problems associated with the trade-off between clinical sensitivity and clinical specificity in screening tests, but also because of the difficult clinical validation in case of a condition like dementia, which contains a broad spectrum of phenotypic variation. The new risk classification schema should be informed by a horizon-scanning exercise to identify the range of new tests being developed which may not have been considered during the development of the GHTF model. Looking to the future, the classification of novel and ambiguous tests will need an EU-level body that is capable of responding with a harmonized decision within short notice, thus enabling the prompt implementation of decisions taken in order to avoid market disruption. Decisions made by individual notified bodies or competent authorities would be liable to result in inconsistency.

Both a EuroGentest document and a document from the European Society of Human Genetics (Eurogentest, 2010; ESHG, 2010) advance that the Directive should be revised in order to address the problems arising from DTC genetic tests on an EU-wide basis. The EuroGentest document believes that concerns about the quality of service and lack of medical supervision should be addressed by identifying those tests which may be made available on a direct-to-consumer basis and those which may only be provided under medical supervision. This should not only be done for genetic tests but for all IVD devices. DTC advertising of tests which are classified as prescription-only should be illegal. The Eurogentest document suggests that the following types of genetic tests should, without exception, be classified as prescription-only: diagnostic tests (i.e. tests intended to diagnose a medical condition in a person with symptoms and/or signs); pre-symptomatic tests (i.e. tests intended to predict that an asymptomatic person has a high probability of developing a condition), carrier tests (i.e. tests intended to show that a person is a carrier of a condition, so that although they are not themselves affected, there is a risk they may have affected children). In parallel, this document advances that, in some cases, tests could be made available DTC: susceptibility/predisposition tests (i.e. tests intended to predict the absolute lifetime risk of an individual developing a condition, where the probability is relatively low compared with the types of risks identified by pre-symptomatic tests) and nutrigenetic tests (i.e. tests used to provide information about how an individual responds to a particular nutrient or diet. However, the EuroGentest response also advanced that susceptibility tests for serious or potentially fatal diseases should not be available DTC (e.g. for cancer or stroke), particularly where the test may cause undue anxiety or may result in serious preventive measures (e.g. prophylactic surgery in case of cancer). Although arguments can be brought to try to distinguish between genetic tests that could be classified as prescription-only and genetic tests that could be provided directly-to-consumers, such a clear-cut classification is difficult to make. Therefore, the document of the European Society of Human Genetics pleads in favour of channeling all health-related genetic tests through medical supervision. In its recent statement on *Direct-to-consumer genetic testing for health-related purposes,* the European Society of Human Genetics stated that "The offer of genetic tests providing health-related information, in the absence of clinical indications and individualized medical supervision, may compromise patient health. Key concerns are the provision of sufficient information about the purpose and appropriateness of testing, its possibilities and limitations, as well as the clinical significance of testing. An involvement of independent medical professionals could avoid the waste of money on tests that are clinically irrelevant. In addition, the cost and adverse psychosocial effects of unnecessary follow-up or medical investigations could be avoided" (ESHG, 2010). Whether or not genetic tests are provided directly-to-consumers or directly-to-doctors, rule 3 of the GHTF risk-classification model should be followed in order for concerns about the quality of the tests to be addressed by subjecting them to a pre-market review that will ensure truth-in-labelling and truth-in-promotion.

3. International framework on the provision of genetic tests[7]

In Europe, an additional protocol to the European Convention on Human Rights and Biomedicine was approved by the Committee of Ministers of the Council of Europe on 7 May 2008 concerning genetic testing for health purposes (Council of Europe, 2008) . This additional protocol deals partly with direct to consumer services. In Article 7.1., this document states that "a genetic test for

[7] Based on Borry P. Europe to ban direct-to-consumer genetic tests? Nat Biotechnol 2008; 26(7):736-737.

health purposes may only be performed under individualized medical supervision." As we can read in the explanatory report, this article has been "driven by the concern to enable the person concerned to have suitable preliminary information with a view to an informed decision regarding the carrying out of this test and, if appropriate, to have access to an appropriate genetic counseling. A precise evaluation of the situation of the person concerned, involving direct contact with him or her, is a determining element in that respect. A mere telephone conversation with a medical doctor, for example, does not allow for such evaluation" (Council of Europe, 2008). If this restriction is enacted in the various Member States, this might create limitations to companies currently offering direct-to-consumer services. Among other issues, this additional protocol emphasizes the importance of genetic counseling, free and informed consent, protecting those unable to give their consent, the right to privacy and the right to information. This additional protocol should be read in relation with the original Convention. In total, out of the 47 Member States of the Council of Europe, 35 have signed and 28 have ratified (http://conventions.coe.int/Treaty/Commun/ChercheSig.asp?NT=164&CM=8&DF=5/19/2008&CL=ENG) the original Convention to date. Ratification is needed before a State can be bound by a treaty. Belgium has not signed and ratified it yet. It is not possible to sign and ratify the additional protocol unless the original convention has been signed and ratified. However, it is possible to take over some of the content of the original convention and the additional protocol in separate legislations. This is for example what various European countries have done (see below).

4. National legislation on the provision of genetic tests[8]

Various European countries have legislation that provides a well-elaborated regulatory framework for the provision of genetic tests. Here, we focus on the existing legislation in France, Germany, Switzerland and Portugal and on how these regulatory frameworks have framed DTC genetic testing.

France

In France, genetic tests are well described and framed in the context of health and this legislation could apply to the DTC context. According to French Law (Article 16-1 Civil Code), genetic tests can only be performed for an individual for "medical or scientific research purposes". When carried out in a medical context, the genetic analysis should be carried out with one of the following goals: (a) to give, confirm or refute the diagnosis of genetic disease in an individual; (b) to detect characteristics of one or more genes, which may be the cause of developing a disease by a person or family members potentially affected; or (c) to adapt the medical care of a person according to his/her genetic characteristics (Article R1131-1 Public Health Code). As a consequence, it is not possible to have access to genetic tests for any another purpose in France, for example simply to obtain information. Moreover, the Public Health Code provides some complementary provisions with regard to (a) the quality of laboratories and scientist training and (b) the mandatory medical relationship. Firstly, in order to perform genetic tests in France, laboratories need to be granted specific authorization delivered for a 5-year period, by the Head of the Regional Agency for Health after consultation with the Biomedicine Agency (Article R1131-14, Public Health Code). In the same way, geneticists must meet a specific requirement to perform genetic tests. They must be specifically trained to be able to verify the results of a genetic analysis (Articles R1131-6 and R1131-7, Public Health Code). Secondly, the use of genetic tests in the clinical context means that the relationship between the user (patient) and the provider (medical doctor) should be defined as a 'medical relationship'. Any other use outside of this context is illegal and cannot be covered by the following provisions. The French law lays down the details on meeting various obligations regarding the terms according to which information should be provided to the patients (or their family), the tests should be prescribed and the results announced (Articles R1131-4 and following). The law is also strict on the requirements for

[8] The description of the legal provisions from the different countries described are taken over from Borry P, van Hellemondt R, Sprumont D, Fittipaldi Duarte Jales C, Rial-Sebbag E, Spranger TM et al. Legislation on direct-to-consumer genetic testing in seven European countries. in review 2011.

consent, which must be obtained in writing after the patient has been informed on the nature and the purposes of the test. This regulation stresses the importance of the information delivered by a medical doctor or the explaintions provided by a genetics counsellor being of high quality. During the revision process of the French Bioethics law (Loi n° 2004-800 du 6 août 2004 relative à la bioéthique, JO n° 182 du 7 août 2004 modifiant la Loi n° 94-653 du 29 juillet 1994 relative au respect du corps humain et la Loi n° 94-654 du 29 juillet 1994 relative au don et à l'utilisation des éléments et produits du corps humain, à l'assistance médicale à la procréation et au diagnostic prénatal), some of the preparatory reports underlined the need to elaborate specific provisions with regard to DTC genetic testing. Considering that DTC tests are sold at an international level and that anticipating the scope of the consumer demand in France will be very difficult, these reports have encouraged the legislator to adopt two kinds of provisions. The conclusions of the reports proposed that, first, prohibition for individuals to use the results of these tests in France should be enshrined in law and, second, that the Biomedicine Agency should be tasked with monitoring the websites offering these tests to ensure their quality and validity. (Office parlementaire des choix scientifiques et technologiques (« L'évaluation de l'application de la loi du 6 août 2004 relative à la bioéthique », 20 novembre 2008), Agence de la biomédecine (« Le bilan d'application de la loi de bioéthique du 6 août 2004 », 2008) ; mission d'information sur la révision des lois bio éthiques (Rapport d'information n° 2235 déposé le 20 janvier 2010).
Finally, the new Bioethics law which entered into force on July 7th, 2011(Law n°2011-814 of July the 7th 2011, published JORF n°0157 July the 8th 2011, page 11826) has implemented most of these proposals. The most significant of these is that, from the perspective of individual rights, the French Public Health code for the first time prohibits individuals from requesting a genetic test for themselves, or for a third person, or for identification through their DNA profile, outside the conditions laid down by the law (Article L.1133-4-1). This action is punishable under Article 226-28-1 of the Criminal Code by a fine of 3.750 Euro. Second, from the institutional perspective, the French Bioethics law reinforces the conditions to be fulfilled by the laboratories that perform genetic tests. In particular, the new Article L. 1131-2-1 (Public Health Code) specifies that only authorized and accredited laboratories may analyse the genetic characteristics of a person, or identify a person through their DNA profile (which excludes companies which are not considered as laboratories). Finally, the Biomedicine Agency is unlikely to be in charge of website surveillance, this being difficult to manage. Nevertheless, the new law tasked the Agency with a new mission, which is to "make information about the uses of direct to consumer genetic tests available to the public and to elaborate a benchmark for the evaluation of their quality" (Article L. 1418-1 paragraph 9, Public health code). The law does not lay down the modalities for implementing this measure. It will be the Biomedecine Agency that will be in charge of acting as an independent body and choosing the best way to ensure and fulfil this mission.

Germany
In Germany, there is no legislation that specifically addresses the issue of DTC genetic testing. However, on 24 April 2009 the German Bundestag passed the Human Genetic Examination Act (The Genetic Diagnosis Act, GenDG) (Bundesrat, 2009), which covers some aspects of these genetic testing services. A prior aim of this law, which came into effect on the 1st of February 2010 (Sec. 27 para. 1; for divergences see sec. 27 paragraph 2 to 4), is on the one hand enhancing the right to informational self-determination concerning the carrying-out of diagnostic or predictive genetic tests, and on the other hand, protecting against abusive use of the information obtained from genetic testing and screening. The Act however focuses on tests carried out under specific circumstances. As art 2 sec. 1 points out, the act only applies to genetic examinations and genetic analyses conducted within the framework of genetic examinations involving born natural persons, as well as embryos and foetuses during pregnancy and the handling of genetic data and genetic samples gained thereby for medical purposes, for purposes of determining descent as well as in the insurance and employment sectors. This Act does not apply to genetic analyses or the handling of genetic samples or genetic data for research purposes, nor does it concern applicable regulations relating to criminal procedures or the Infection Protection Act.

According to sec 7 paragraph 1 of the Act, a diagnostic genetic examination may only be undertaken by physicians and a predictive genetic examination may only be performed by medical specialists in the field of human genetics or other physicians who have qualified themselves via the acquisition of some specialist designation for genetic examination within their specialist area. Paragraph 2 states that the genetic analysis of a biological sample may only be carried out within the scope of a genetic examination and by the medical person in charge or by a person or institution commissioned by the medical doctor in charge. Paragraph 3 finally holds that genetic counselling according to sec 10 may only be undertaken by physicians named in paragraph 1 and who are qualified to provide genetic counselling.

Furthermore, a precondition for valid informed consent is the clarification presented in sec. 9 para. 1-3: "Before obtaining consent, the medical person in charge must inform the person concerned on the nature, meaning and consequences of the genetic examination. After being informed the person concerned must receive sufficient time for consideration before deciding to provide consent. The clarification covers in particular: (1) the purpose, type, scope and significance of the genetic examination including the results attainable in the course of the purpose of the examination and with the designated means of examination; the foregoing also includes any genetic characteristics which are to be examined and which are significant in terms of avoiding, preventing or treating any illness or health condition; (2) the health risks for the person concerned which are connected to the knowledge of the results of the genetic examination and the procurement of the necessary biological sample (…); (3) the intended use of any sample as well as the results of any genetic examination or analysis; (4) the right of the person concerned to revoke his or her consent at any time; (5) the right of the concerned person to not have to know results (…)."

Under this legislation, the DTC provision of genetic tests is clearly restricted in Germany. Genetic tests can only be carried out by a medical doctor after having provided sufficient information concerning the nature, meaning and consequences of the genetic test and after the person concerned has given his/her consent. The German law described in this section does not regulate tests for research purposes, but companies cannot simply circumvent this legislation by suggesting that their tests are for research and educational purposes only. However, the mere selling of test kits and the application of DTC GT outside the areas described are not prohibited per se, and individuals purchasing tests from abroad will not be penalized. Finally, it must also be noted that the legal debate over the DTC issue has only just begun, which means that many questions are still open. In particular, the relevance of self-determination as a legal concept and the degree to which German law requires the person concerned to be protected from his/her own decisions remains to be clarified.

Switzerland

In Switzerland, the conditions under which human genetic testing may be performed are regulated under the *Federal Act on Human Genetic Testing* (Federal Assembly of the Swiss Confederation, 2004) from 8 October 2004 (Sprumont, 2004). The genetic tests offered directly-to-consumers correspond to the definition of 'genetic in vitro diagnostic medical devices' as formulated by Article 3j of the above mentioned law: "ready-to-use products for the determination of characteristics of human genetic material". These tests are covered by Article 9 of this Act, which reads as follow: "(1) It is forbidden to supply genetic in vitro diagnostic medical devices to individuals for a purpose which cannot be considered part of those individuals' professional or commercial activities; (2) The Federal Council may, having consulted the Expert Commission for Human Genetic Testing, make provision for exceptions to this prohibition provided the products are used under medical supervision and misinterpretation of the test result is not possible."
The Act has been completed by two ordinances: the Federal Council Ordinance on Human Genetic Testing from 14 February 2007 (Federal Assembly of the Swiss Confederation, 2007) and the Federal Department of Home Affairs Ordinance on Human Genetic Testing from 14 February 2007 (Federal Department of Home Affairs, 2007). None of these regulations provide for an exception to Article 9 of the Act prohibition for DTC genetic testing. To the best of our

knowledge, no request has been submitted to the competent authorities to date to obtain the right to benefit from the exceptions mentioned in the Act. One could therefore conclude that such tests remain unlawful in Switzerland.
In fact, the Act makes it a criminal offense to infringe this prohibition as stated in Article 38: "(1) Any person who, in contravention of Article 9 paragraph 1, wilfully supplies genetic in vitro diagnostic medical devices to individuals for a purpose which cannot be considered part of those individuals' professional or commercial activities shall be liable to a fine; (2) If the act is committed for commercial gain, the penalty shall be a custodial sentence not exceeding three years or a monetary penalty."
Yet, it should be underlined that the prohibition or at least the severe restriction imposed by the law is limited to putting these devices on the market, and does not apply to their use. The law does not provide for any explicit sanctions against those who import such tests for their own personal use. The issue is indeed very similar to that of importing therapeutic products of any kind. In practice, this is tolerated by the law as long as it remains limited to personal use and does not present a risk in terms of public health. For genetic testing, there is also another dimension as there are many companies advertising on the Internet that offer simple and rather inexpensive paternity tests (Sprumont, 2003). The key point in this case is that the test requires testing not only the potential father(s) but also the child. When the latter is a minor, there is a clear conflict of interest in the "father" consenting on behalf of the child, especially when he is not actually the legal father. Courts have already ruled that such tests are invalid and may not be used to challenge the family relationships between a man and a child. There could also be an issue of liability, as the test could be considered as an infringement of the personal rights of each person whose DNA is analyzed without their consent (Büchler, 2005) – without mentioning the rights of the legal parents if their family relationship is refuted – and therefore pave the way for obtaining indemnities.

Portugal

In Portugal, the Law n°12/2005 of 26 January 2005 defines the concept of health information and genetic information, and sets forth rules for the collection and preservation of biological products for genetic testing for clinical or research purposes. In Article 10 of this law, different genetic tests are categorized based on use: tests to be used for the detection of carriers of recessive disorders; pre-symptomatic tests for monogenic diseases; predictive tests allowing the detection of susceptibility genes; pharmacogenetic tests; prenatal tests and tests used for screening. According to Article 9.2 of the Law nº12/2005, the detection of the heterozygosity status of recessive diseases, the presymptomatic diagnosis of monogenic diseases and the tests for genetic susceptibility in healthy persons can only be carried out upon request from a medical geneticist, following a genetic counselling consultation and subject to the express written and informed consent of the person in question. Article 9.7 also advances that when there is a risk of severe, late-onset diseases that appear in early adulthood and for which there is no cure or proven effective treatment, the carrying out of any presymptomatic or predictive testing must be preceded by a previous psychological and social evaluation and requires patient follow-up after the delivery of the test results. Besides, Article 17.3 also states that every citizen has the right to receive genetic counselling and, if appropriate, psychological and social support, before and after heterozygosity, presymptomatic, predictive or prenatal genetic tests. In this context, it is also important to state that Portugal ratified the Oviedo Convention (Council of Europe, 1997), through Presidential Decree nº 01/2001, which means that the aforementioned Convention has force of law throughout the national territory. According to Article 12 of this convention, "tests which are predictive of genetic diseases or which serve either to identify the subject as a carrier of a gene responsible for a disease or to detect a genetic predisposition or susceptibility to a disease may be performed only for health purposes or for scientific research linked to health purposes, and subject to appropriate genetic counselling" (Council of Europe, 1997). Finally, in July 2008, the National Council of Ethics for the Life Sciences issued an opinion according to which genetic testing for health purposes should not be offered directly to the public, in compliance with fundamental ethical principles. This document is not a legally binding document.

Based on these provisions, various jurists advance that DTC genetic testing is forbidden in Portugal (Sequeiros, 2011). However, Article 15 of Law nº 12/2005 still confers to the Government the responsibility of regulating the conditions under which genetic tests should be available and conducted. The aim is to prevent tests from being made available by national or foreign laboratories that do not have the support of a proper and multidisciplinary medical team, and to avoid the possible over-the counter marketing of this type of tests. Notwithstanding this legal provision and an Order, issued in September 2008, by the Ministry of Health, for the creation of a task group in charge of regulating the Law nº 12/2005, there are still no regulations that determine measures for accreditation, certification and licensing of public and private laboratories responsible for genetic testing. As a consequence, no specific legislation addressing DTC genetic testing has been enacted yet and, according to some authors, there are no real legal provisions prohibiting DTC genetic testing services.

Belgium

In Belgium, no specific legislation forbids or regulates the provision of DTC genetic tests. A Royal Decree of 14 December 1987 (Published in the Belgian Official Gazette of 25 December 1987) lays down the rules for the provision of genetic testing in the Centres for medial Genetics in Belgium. Additionally, the Royal Decree of June 7th, 2007, modifying the Royal Decree of September 7th, 1984, sets requirements for laboratories performing reimbursed molecular biological tests for the determination of acquired pathologies in human genetic material. The only legal basis applying to DTC genetic tests could be found in Article 2 of the Law on the practice of healthcare professions (Royal decree n°78 (Belgian Official Gazette of 14.11.1967)) [9], which stipulates that a physician shall be involved in the practice of medicine. It follows that, if a given DTC genetic test falls under the practice of medicine, a physician shall be involved and the Law on patient rights shall apply. In this respect, it is important to determine whether a DTC genetic test could be considered as pertaining to the 'practice of medicine'. As we know, most DTC companies write in their 'terms of services' that they do not practice medicine, and that their tests should not be considered medical information, but that they only serve "informational purposes." Whether or not this statement would stand further legal or judicial scrutiny has yet to be proven.

In Flanders, the Flemish regulatory framework on screening has been laid down in the Flemish Parliament Act of 21 November 2003 concerning the preventative health policy. Within the framework of disease prevention and based on the Decision of the Flemish Government of 12 December 2008 on population screening in the framework of the prevention of illness, Flanders organizes population-based screening programmes, which are generalized and structured forms of detection, or screenings for specific diseases or risks in people who are, in principle, free of health complaints. This method allows for early diagnosis and thus for either obtaining better treatment results, or preventing complications. The Flemish Government aims to protect the population against unessential or unproven screening and to ensure the quality of population based screenings. Although DTC genetic testing might fall under this regulatory framework, the Flemish authorities (until now) have not stipulated that DTC genetic tests fall under this legislation. That being said, if healthcare professionals or pharmacists are involved in the provision of DTC tests, this practice does fall under this legislation.

[9] Article 2: **[**Koninklijk besluit nr 78 betreffende de uitoefening van de gezondheidszorgberoepen] "Niemand mag de geneeskunde uitoefenen die niet het wettelijk diploma bezit van doctor in de genees-, heel- en verloskunde, dat werd behaald in overeenstemming met de wetgeving op het toekennen van de academische graden en het programma van de universitaire examens, of die niet wettelijk ervan vrijgesteld is, en die bovendien de voorwaarden gesteld bij artikel 7, (...) niet vervult."

5. Screening legislation[10]

The Netherlands has no legislation that specifically addresses DTC genetic testing (van Hellemont et al., 2011). In principle, companies are allowed to offer DTC genetic tests to the public. However, the Dutch Act on population screening (henceforth Act), by way of a licence system, seeks to protect individuals against screening programmes that pose a potential health threat. This legal framework was introduced to establish and guarantee a fair balance between individuals' right to self-determination and the need to protect them against (potentially) harmful screening programmes (Van der Maas et al., 2000). Hence, although the Act on population screening was not developed to regulate the access and the use of DTC genetic tests specifically, it does apply to certain of these tests.

In this Act, population screening is defined as "a medical examination which is carried out in response to an offer made to the entire population or to a section thereof and to detect diseases of a certain kind or certain risk indicators, either wholly or partly for the benefit of the persons examined'. The key word in the definition is *'offer'*. DTC genetic tests which predict diseases based on risk indicators fit within this definition due to the fact that companies advertise and offer their genetic tests directly to the public in magazines, newspapers and through the Internet. The fact that individuals visit the website or the web shop of 'test companies' on their own initiative makes no difference when classifying DTC genetic tests as population screening.

According to the Act, some forms of DTC genetic tests can only be carried out with a permit issued by the Dutch Minister of Welfare and Sports. Offering and carrying out DTC genetic tests for detecting (risk factors of) cancer and (risk factors of) 'incurable' diseases –which can neither be treated nor prevented- without a licence is against the law in the Netherlands. Moreover, performing these tests without permission is a punishable offence (Article 3 (1) and Article 13). Based on Article 7, the Dutch Minister in charge can refuse to grant a licence if a test is scientifically unsound, is not in accordance with the professional medical practice standards or if the expected benefit is not in balance with the (potential) health risks. The Act does not set up quality norms for the information to be provided to the consumers of DTC genetic tests, nor for the consent to use samples and the counselling to be provided to the customers. Nevertheless, DTC genetic testing companies wishing to sell genetic tests for detecting (risk factors for) cancer and (risk factors for) 'incurable' diseases have to comply with the professional medical practice standards, which include the protection of the main patients' rights laid down in the Dutch Civil Code.

Furthermore, the Dutch 'Medical Treatment Contracts Act', as part of the Dutch Civil Code, applies to all contracts whereby a healthcare provider undertakes to provide medical services. The main purpose of this 'Act' is to clarify and strengthen the legal position of the patient. It lays down the rights and obligations of care providers and the patient. Among other things, it sets up quality norms for the information to be provided, for obtaining consent and handling confidential patient data. According to the 'Medical Treatment Contracts Act', healthcare providers have to give information about the indication, the proposed treatment, alternatives, prognoses, risks and possible side-effects prior to initiating a medical intervention. The Dutch licence system guarantees normative criteria for DTC genetic tests aimed at detecting (risk indicators of) cancer and (risk indicators of) 'incurable' diseases. This legal framework effectively prevents individuals from gaining access to some DTC genetic tests with a questionable validity and clinical utility in the Netherlands.

However, from the beginning there was confusion about the scope of the Act, and thus uncertainty about the requirement of obtaining a licence. The Health Council -a scientific advisory body- has been allotted the task of advising the Minister on the provision of a licence to applicants under the Act (Article 6). The Dutch Health Council has written several reports to clarify the scope of the Act. Despite these helpful reports certain uncertainties remain that are probably inherent to the use of terms like 'population screening', 'offer' and 'incurable'. In the light

[10] The description of the legal provisions in the Netherlands is taken over from Borry P, van Hellemondt R, Sprumont D, Fittipaldi Duarte Jales C, Rial-Sebbag E, Spranger TM et al. Legislation on direct-to-consumer genetic testing in seven European countries. in review 2011.

of these difficulties, there was already a call to revise the Act to enhance its effectiveness over 10 years ago (Van der Maas, 2000).

Flanders too has an Act on Screening. However, in contrast to the Dutch regulatory framework, the Flemish authorities do not consider DTC genetic tests to fall under the application of the Flemish Act on Screening at the moment (unless they are provided by healthcare professionals or pharmacists). In Wallonia or Brussels, no legislation is in place that regulates the provision of DTC genetic tests in the context of screening legislation.

6. Implementation of existing legislation on information services[11]

In this context, the advice elaborated by the Belgian Advisory Committee is relevant: "As regards the bringing of genetic tests onto the market in Belgium via the Internet, reference should be made to the law of 11 March 2003 on certain legal aspects of the services of the information society (*Belgian Official Gazette* of 17.03.2003) and relevant royal decree of enforcement of 7 May 2003 (*Belgian Official Gazette* of 07.07.2003), as well as the law of 8 December 1992 for the protection of personal privacy, in respect of the processing of personal data (*Belgian Official Gazette* of 18.03.1993). The law of 11 March 2003 is applicable to all "information services". This therefore concerns all services provided by electronic means, i.e. which are originally sent and received by the recipient with the aid of computer equipment, even if for example a part of the service is provided physically. Predictive genetic tests sold via web sites fall under this law, even if the blood samples or results are sent by post. Pursuant to Article 5 of this law, the provision of information society services by a service provider established in Belgium must comply with the requirements in force in this country. Therefore, every site which offers this kind of service and is established in Belgium is subject to Belgian law and in particular to the law on the protection of privacy (*confer infra*). The Royal Decree of 7 May 2003 implementing the law of 11 March 2003 moreover determines that the services of the General Board of Control and Arbitration of the federal Department for Economic Affairs can take specific measures for the limitation of the free traffic of an information society service offered by a provider established in another European Union Member State. In addition to the fairly cumbersome procedure which this rule provides for, the limitation solely to web sites established on the territory of EU countries clearly significantly curtails its scope. As regards sites which sell genetic tests and are not established in Belgium but can be accessed from this country, the Law of 11 March 2003 in some cases makes it possible for service providers who "host" these sites to be held liable. A "site host" established in Belgium with sites on which genetic tests are offered for sale could be held liable if it did not take prompt action to remove the information or render access to it impossible as soon as it became aware of the illegal nature of the activity or information on its server. Data such as the biological samples needed to carry out a genetic analysis constitute personal data that fall within the scope of the Law of 8 December 1992 on the protection of privacy in relation to the processing of personal data. This law is applicable to the processing of personal data within the framework of activities by a body established in Belgium (site selling genetic tests which is established in Belgium), but also when the party responsible for processing the personal data is not established within the European Union, but calls upon automated or non-automated resources which are located in Belgium for the processing of personal data. All cases of genetic data collected on Belgian soil by sites selling genetic tests consequently fall within the scope of the law, irrespective of the nationality of the person concerned. The Law and its implementing Decree of 13 February 2001 (Belgian Official Gazette of 13.03.2001) lay down a number of principles that apply to all processing of personal data. For example, these texts regulate the way in which the collected data should be stored, as well as the subsequent use that is made of them. But for the person concerned to give their consent, personal data on health may only be processed under the responsibility of a professional practitioner in the healthcare sector and certain information should be given to the person concerned at the time these data are collected. The Law provides for

[11] This section has been copied from: Belgian Advisory Committee on Bioethics. Opinion no. 32 of 5 July 2004 on the free availability of genetic tests. 2004. www.health.fgov.be/bioeth.

penalties for failing to observe the legal provisions. The same principles for the protection of personal data are applied in other countries of the European Union. These principles are based on European directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data. ”

7. Information provision to healthcare professionals and the general public

As with any new market, the commercial success for DTC GT companies will depend greatly on the public demand for these services. This consumer demand will in turn depend on many factors, including consumers' desire or need to obtain genetic testing services outside of the traditional healthcare system. With this in mind, the DTC model of genetic testing may have underestimated the consumer's attachment to their physician. A report by the investment bank Burril & Company (San Francisco) revealed that physicians remain the most likely source to which individuals will turn for health and genetic information (www.burrillandco.com). A few studies also showed that two thirds of consumers who ordered DTC genetic tests shared their test results with their healthcare professional or were planning to do so (McGuire et al., 2009). In general, the DTC model raises concerns in potential consumers over the reliability of the tests, security issues as regards the use made of their DNA,as well as the privacy of genetic risk information, and generates a lack of confidence in non face-to-face genetic counseling (Wilde et al., 2010). Bearing this in mind, it is not surprising that some companies have recently opted for DTC *advertising* instead of selling their services directly-to-consumers. They have combined DTC advertising with the involvement of regular healthcare professionals, who then order the test for their patients. Depending on the test, some companies require an order from a physician (e.g. www.hairdx.com) or an oncologist (e.g. www.collabrx.com). The company Counsyl, (www.counsyl.com) which offers pre-conceptional carrier testing, has changed its policy since its launch in February 2010. At the time, Counsyl underlined the possibility of ordering the test directly from the company: “You can order the test directly from our website to receive your kit immediately. Everyone has a prescription: the American College of Medical Genetics (ACMG) recommends that adults of reproductive age be offered carrier testing for cystic fibrosis and spinal muscular atrophy, two of the many conditions assayed by the Universal Genetic Test. Alternatively, you may get the test through your doctor.” (https://www.counsyl.com/learn/easy/ accessed 04/05/2010) Since May 2010, however, testing from Counsyl can only be requested through a physician and therefore consumers first need to find a physician who will prescribe the test. The company also sends the results directly to the physician for interpretation, thereby, technically no longer selling tests directly-to-consumers. (https://www.counsyl.com/learn/easy/ accessed 06/06/2010). The offer through physicians may put to rest some of the concerns that arose about information provision, but the issue of whether or not the test provided is appropriate remains. In this context, it is increasingly important for physicians to act as a gatekeeper for tests that may prove to be inappropriate. It is therefore concerning that some of these companies provide lists of medical doctors on their website through whom the tests (that are advertised directly to consumers) can be ordered.

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5. COMPOSITION OF THE WORKING GROUP

All experts joined the working group ***in a private capacity.*** The names of the members and experts of the Superior Health Council are indicated with an asterisk*.

The following experts were involved in drawing up the advice :

ANTOINE-POIREL Hélène	Human Genetics - Oncogenetics	UCL
BAATOUT Sarah	Radiobiology	SCK- CEN
BLAUMEISER Bettina	Genetics - Gynecology	UA
BORRY Pascal	Biomedical Ethics	K.U.Leuven
CASSIMAN Jean Jacques*	Human genetics	K.U.Leuven
dE THIBAULT DE BOESINGHE Léopold	Industrial Medecine, oncologist radiotherapy nuclear medecine	UGent - Member of the Consulting Bioethics Committee of Belgium
FONDU Michel*	Chemistry, additives, contaminants	ULB
GODDERIS Lode	Occupational Health Physician, Toxicologist	K.U. Leuven
HAUFROID Vincent	Pharmacogenomics	UCL
HULSTAERT Frank	Medicine	KCE
KIRSCH-VOLDERS Micheline*	Cellular and environmental genetics	VUB
LIEBAERS Inge	Medical Genetics	VUB - former president of the High council on human genetics - Member of the Consulting Bioethics Committee of Belgium
LOEYS Bart	Human Genetics	UA
POPPE Bruce	Medical Genetics	UGent
SCHAMPS Geneviève,	Biomedical Law	UCL - Member of the Consulting Bioethics Committee of Belgium
VAN LAREBEKE Nicolas	Carcinogenesis and cancer prevention	UGent
VAN NEROM Anne	IVD competent authority	Scientific Institute of Public Health
VAN OYEN Herman*	Public Health, epidemiology	Scientific Institute of Public Health
VERELLEN-DUMOULIN Christine	Human Genetics	UCL, IPG
VIKKULA Mikka	Molecular Human Genetics	UCL

The working group was chaired by Herman VAN OYEN, the scientific secretary was Sylvie GERARD

Over de Hoge Gezondheidsraad (HGR)

De Hoge Gezondheidsraad is een federaal adviesorgaan waarvan de FOD Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu het secretariaat verzekert. Hij werd opgericht in 1849 en geeft wetenschappelijke adviezen i.v.m. de volksgezondheid aan de ministers van Volksgezondheid en van Leefmilieu, aan hun administraties en aan enkele agentschappen. Hij doet dit op vraag of op eigen initiatief. De HGR probeert het beleid inzake volksgezondheid de weg te wijzen op basis van de recentste wetenschappelijke kennis.

Naast een intern secretariaat van een 25-tal medewerkers, doet de Raad beroep op een uitgebreid netwerk van meer dan 500 experten (universiteitsprofessoren, medewerkers van wetenschappelijke instellingen, praktijkbeoefenaars, enz.), waarvan er 300 tot expert van de Raad zijn benoemd bij KB; de experts komen in multidisciplinaire werkgroepen samen om de adviezen uit te werken.

Als officieel orgaan vindt de Hoge Gezondheidsraad het van fundamenteel belang de neutraliteit en onpartijdigheid te garanderen van de wetenschappelijke adviezen die hij aflevert. Daartoe heeft hij zich voorzien van een structuur, regels en procedures die toelaten doeltreffend tegemoet te komen aan deze behoeften bij iedere stap van het tot stand komen van de adviezen. De sleutelmomenten hierin zijn de voorafgaande analyse van de aanvraag, de aanduiding van de deskundigen voor de werkgroepen, het instellen van een systeem van beheer van mogelijke belangenconflicten (gebaseerd op belangenverklaringen, onderzoek van mogelijke belangenconflicten en een Commissie voor Deontologie) en de uiteindelijke validatie van de adviezen door het College (eindbeslissingsorgaan van de HGR, samengesteld uit 40 leden van de pool van benoemde experten). Dit coherent geheel moet toelaten adviezen af te leveren die gesteund zijn op de hoogst mogelijke beschikbare wetenschappelijke expertise binnen de grootst mogelijke onpartijdigheid.

Na validatie door het College worden de adviezen overgemaakt aan de aanvrager en aan de minister van Volksgezondheid en worden ze gepubliceerd op de website (www.hgr-css.be). Daarnaast wordt een aantal onder hen gecommuniceerd naar de pers en naar bepaalde doelgroepen (beroepsbeoefenaars in de gezondheidssector, universiteiten, politiek, consumentenorganisaties, enz.).

Indien u op de hoogte wilt blijven van de activiteiten en publicaties van de HGR kunt u een mail sturen naar info.hgr-css@health.belgium.be.