CytoCell

A Sysmex Group Company

Microdeletion and Prenatal FISH Probes

Features

- Improve confidence in result interpretation with high intensity signals and minimal background
- Enhance detection and scoring accuracy with robust, easy-to-analyse probes
- Save time and minimise mixing errors with easy-to-use, pre-mixed probes
- Optimise stock levels and minimise wastage with flexible pack sizes to meet your needs
- **New!** IVDR-certified FISH probes for added safety and confidence

Microdeletion Testing

Microdeletion syndromes are a group of clinically-recognisable disorders brought about by the deletion of specific regions of chromosomal DNA, causing haploinsufficiencies of important genes. These deletions are difficult to visualise using standard cytogenetic techniques such as karyotyping, however FISH can resolve these submicroscopic deletions.

Our comprehensive range of microdeletion probes include products for some of the rarest human genetic syndromes. All of our microdeletion probes are available in economical 5, or standard 10 test kits.

Why Choose CytoCell Probes?

Customers can have confidence in CytoCell's bright, tight signals and minimal background.

The OGT Partnership

Behind every sample is a life that can be improved through the right care decisions.
The OGT partnership approach is key to providing the highest level of service, working closely with you to understand your unique challenges, customising our approach to meet your exact needs. Choose CytoCell probes for your FISH analysis; our effective, accurate and simple to use products help clinical decision makers to reach the right decisions for each patient.

Cri-du-chat/SOTOS Probe Combination

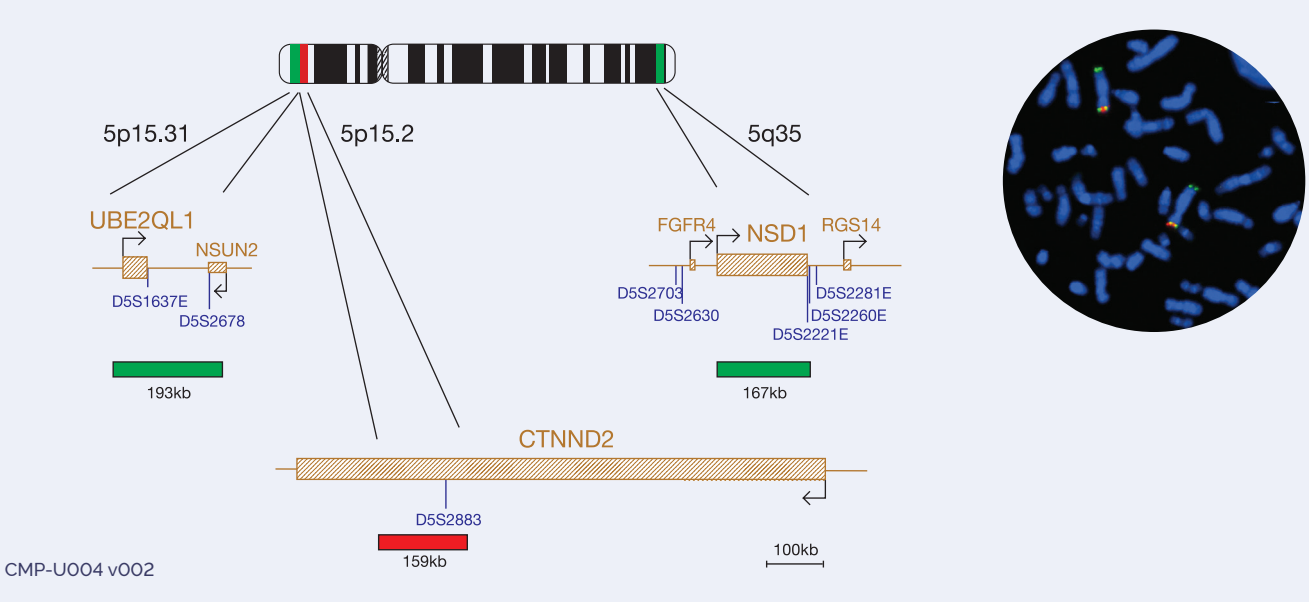
Cat. No. **LPU 013-S** (5 tests) | Cat. No. **LPU 013** (10 tests)

Cri-du-chat syndrome consists of multiple congenital anomalies, mental retardation, microcephaly, abnormal face and a mewing cry in infants. Cri-du-chat Syndrome is associated with deletions, which vary in size, of part of the short arm of chromosome 5[1].

The estimated prevalence varies between 1 in 20,000 to 1 in 50,000 births[2], making it one of the more common deletion syndromes. A critical chromosomal region involved in the high-pitched cry has been mapped to the proximal part of chromosome band 5p15.3[3]. The region involved in the remaining features of the syndrome has been mapped to 5p15.2[3,4,5].

SOTOS syndrome-1 (SOTOS1) is a neurological disorder characterised by a distinctive facial appearance, overgrowth in childhood and developmental delay[6]. Malignant tumour formation has also been reportedly associated with SOTOS1[7].

NSD1, a gene encoding a histone methyltransferase, and implicated in chromatin regulation[8], was identified as the gene disrupted by the 5q35 breakpoint in a patient carrying a chromosomal translocation[9]. The major causes of SOTOS1 are mutations of the *NSD1* gene or deletions of the 5q35 region causing haploinsufficiency of the *NSD1* gene.



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DiGeorge and 22q13.3 Deletion Probe Combinations

DiGeorge Syndrome

DiGeorge syndrome[1], and a variety of congenital malformation syndromes including Velocardiofacial syndrome (VCFS)[2], have in common deletions of chromosome 22 at 22q11.2[2,3,4,5]. These syndromic phenotypes are collectively coined CATCH22, a mnemonic that covers the clinical findings of Cardiac abnormality, Abnormal facies, Thymic aplasia, Cleft palate and Hypocalaemia/Hyperthyroidism due to a chromosome 22 deletion. In addition, around 29% of nonsyndromic patients with isolated conotruncal defects have been shown to have a 22q11.2 microdeletion[6]. The incidence of these anomalies is estimated to be 1:4000 to 1:9700 live births[7] and the deletion of 22q11.2 therefore represents one of the most common genetic defects. A region of approximately 2Mb, referred to as the DiGeorge Critical Region (DGCR), is the most commonly deleted region and occurs in up to 90% of patients[5,8,9]. Within the DGCR, a minimal critical region of 300- 480kb has been described[10,11], containing several genes, including *HIRA* (*TUPLE1*), *TBX1*, *SLC25A1* (*CTP*) and *CLTCL1*.

22q13.3 Deletion Syndrome

The 22q13.3 deletion syndrome presents a recognisable phenotype characterised by hypotonia, delay or absence of expressive speech, global developmental delay, normal to accelerated growth and mild dysmorphic features[12,13]. Some deletions of the terminal region of chromosome 22q are cytogenetically visible. However, a few cases of cryptic deletions have been reported[12,14], suggesting that the actual incidence of 22q telomere deletion may be higher than previously thought. Several observations of patients with 22q13.3 deletion showed that the *SHANK3* (*ProSAP2*)[20] gene, encoding a structural protein of the postsynaptic density of excitation synapses and expressed in the cortex and cerebellum of the brain[15], was disrupted[15,16,17] or deleted[18], making it a candidate causative gene for this syndrome.
The deletion varies dramatically in size from 130kb to 9Mb[18,19,20]. The use of 22q subtelomeric probes, distal to the *ARSA* gene, have therefore been recommended for examining all 22q13.3 deletions[20,21].

References

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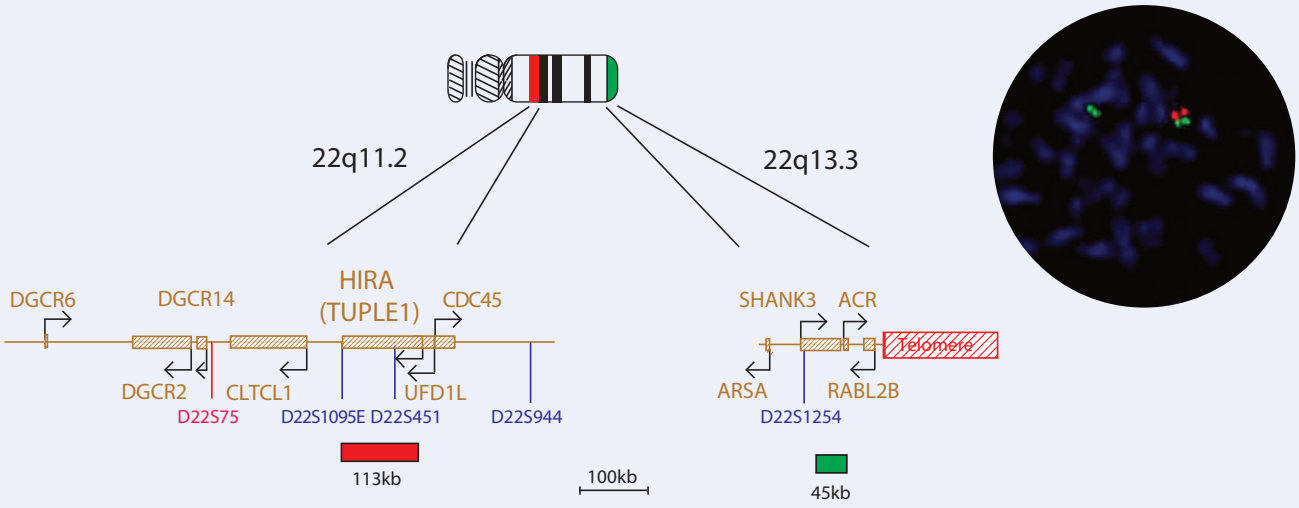
DiGeorge/VCFS TUPLE1 & 22q13.3 Deletion Probe Combination

Cat. No. **LPU 004-S** (5 tests) | Cat. No. **LPU 004** (10 tests)

The TUPLE1 probe is 113kb, labelled in red, and covers most of the *HIRA* (*TUPLE1*) gene. The N85A3 (45kb) probe, labelled in green, is located within 22q13.3 and covers the telomeric end of the *SHANK3* gene. The two unique sequences provide control probes for each other and allow identification of chromosome 22.

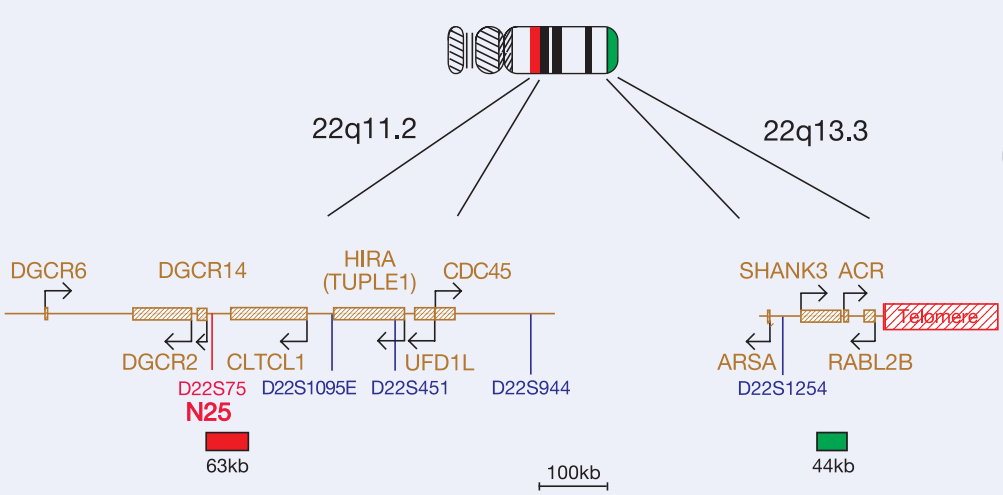


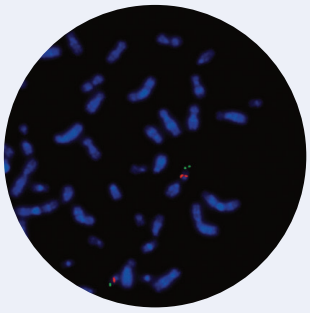
CMP-U008 v006

DiGeorge/VCFS N25 & 22q13.3 Deletion Probe Combination

Cat. No. **LPU 010-S** (5 tests) | Cat. No. **LPU 010** (10 tests)

The N25 probe is 63kb, labelled in red and covers a region including the D22S75 marker and the centromeric end of the *CLTCL1* gene. The N85A3 (44kb), labelled in green, is located within the 22q13.3 band and covers the telomeric end of the *SHANK3* gene. The two unique sequences provide control probes for each other and allow identification of chromosome 22.



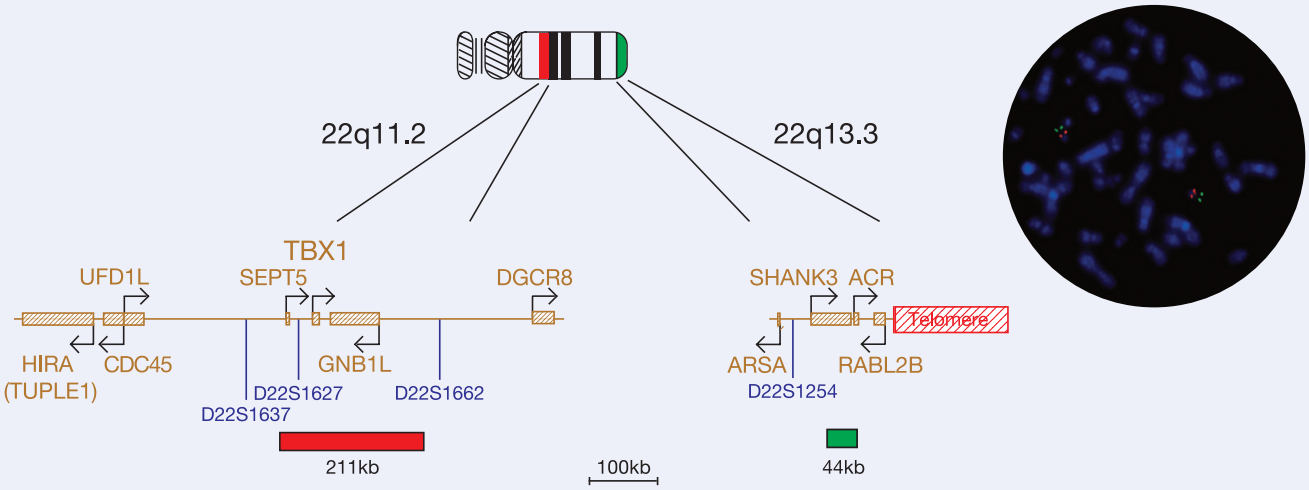


CMP-U007 v003

DiGeorge/TBX1 & 22q13.3 Deletion Probe Combination

Cat. No. **LPU 014-S** (5 tests) | Cat. No. **LPU 014** (10 tests)

The TBX1 probe is 211kb, labelled in red, and covers the entire *TBX1* gene including the D22S1627 marker. The N85A3 (44kb), labelled in green, is located within 22q13.3 and covers the telomeric end of the *SHANK3* gene. The two unique sequences act as control probes for each other and allow identification of chromosome 22.



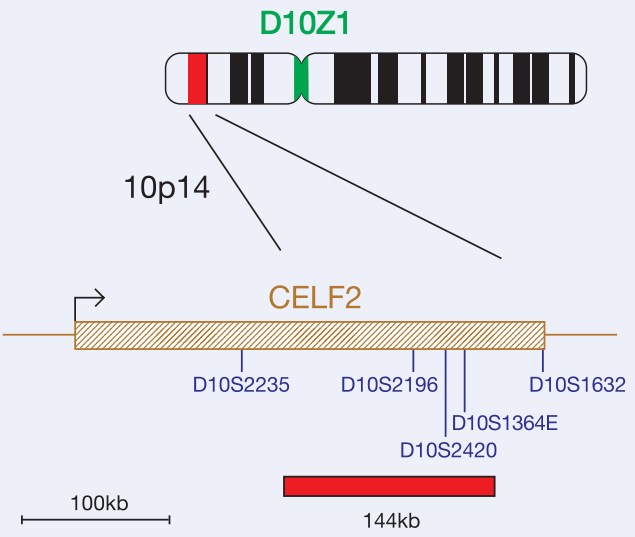
CMP-U006 v003

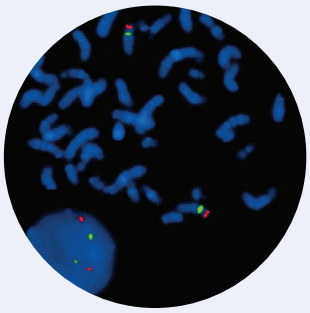
DiGeorge II (10p14) Probe

Cat. No. **LPU 015-S** (5 tests) | Cat. No. **LPU 015** (10 tests)

DiGeorge syndrome[1], and a variety of congenital malformation syndromes including velocardiofacial syndrome (VCFS)[2], share the deletion of chromosome 22 at 22q11.2[2,3,4,5]. These chromosome 22 deletions are collectively coined CATCH22, a mnemonic that covers the clinical findings of Cardiac abnormality, Abnormal facies, Thymic aplasia, Cleft palate and Hypocalaemia/Hyperthyroidism due to a chromosome 22 deletion. In DiGeorge syndrome, however, cases have also been found in which patients have a deletion on chromosome 10p14 (DGS2) instead of chromosome 22[6,7,8].

The deletion of the DGS2 locus on 10p may be 50 times less frequent than that of the DGS1 locus on 22q and has been estimated to occur in 1 in 200,000 live births[9]. The *CELF2* gene has been identified within the 300kb minimally deleted region of DGS2 and is postulated to be involved in the DGS2 deletion[10]. *CELF2* is a candidate gene for the heart defect and thymus hypoplasia/aplasia associated with partial monosomy 10p[10] and may be involved in atrial septal defects (ASDs), a common cardiac anomaly associated with DGS2[11].





CMP-U005 v002

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Prader-Willi/Angelman (SNRPN) Probe

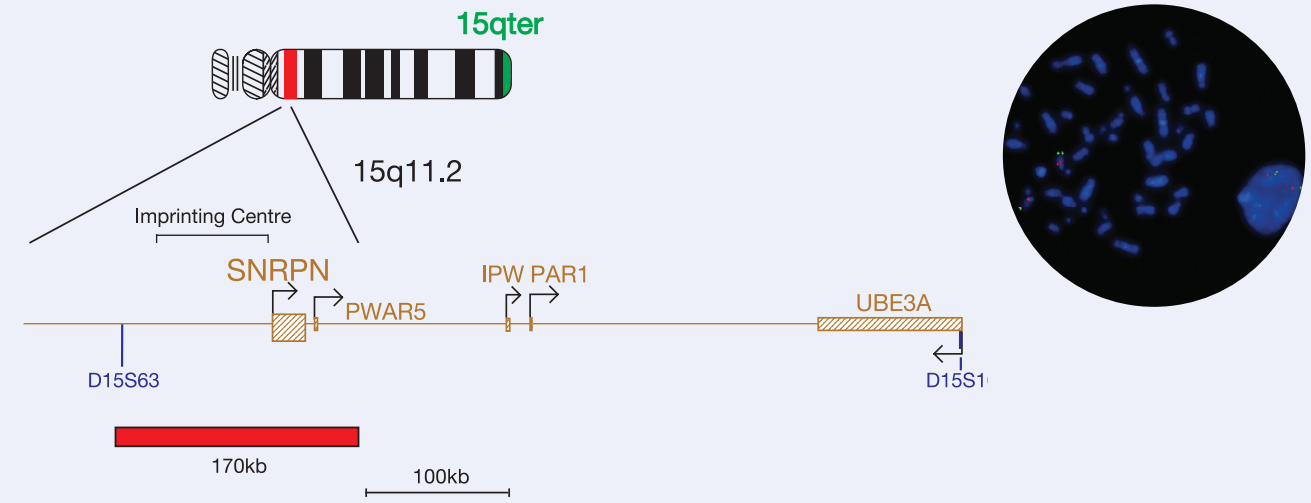
Cat. No. **LPU 005-S** (5 tests) | Cat. No. **LPU 005** (10 tests)

Prader-Willi Syndrome (PWS) and Angelman Syndrome (AS) are distinct neurogenetic disorders caused by the loss of function of genes on chromosome 15 (bands 15q11-13), on either the paternally or maternally inherited chromosome, respectively[1].

In 70% of patients, a large interstitial deletion of 3-4Mb is observed[1,2]. In around 3% of patients, an imprinting defect is observed, caused by either an epimutation or a microdeletion of the Imprinting Centre (IC)[1,3]. Uniparental disomy, in which both chromosome 15s are inherited from the same parent, accounts for most of the remaining patients with PWS/AS[1].

The *SNRPN* gene is one of four imprinted loci that are expressed from the paternal chromosome 15 region (15q11-13) and maps to the minimally deleted region (MDR) involved in PWS[4]. Its chromosomal location and imprinting status suggest it plays a possible role in the aetiology of PWS[5].

The imprinting centre (IC) maps to a 100kb region proximal to *SNRPN*. Parental deletions or mutations in the IC impair the imprinting process in 15q11-13 and cause one of two distinct diseases in their offspring[5,6]. Most of the PWS imprinting deletions involve *SNRPN* and are approximately 200kb in size. The AS imprinting deletions are small (approximately 40kb), involve the BD3 region, and do not include *SNRPN*.



CMP-U013 v002

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Prenatal Testing

The CytoCell prenatal FISH assays are designed for the rapid and accurate detection of the most common foetal chromosomal disorders:

- **Down syndrome[1] (Trisomy 21)**
- **Edwards syndrome[2] (Trisomy 18)**
- **Patau syndrome[3] (Trisomy 13)**
- **Sex chromosome disorders[4] (Copy number changes of X and/or Y chromosomes)**

Prenatal Enumeration Kits

Our Prenatal Kits contain FISH probes for the identification of trisomies 21, 18 and 13, as well as sex chromosome aneuploidies utilising an overnight protocol.

FAST FISH Prenatal Kits

When rapid results really matter, choose CytoCell's *FAST* prenatal FISH probes; utilise our 2-hour hybridisation protocol to meet the demands of urgent turnaround times, without compromising on signal quality.

NEW! IVDR-Certified Prenatal Kit

For added confidence and safety, our prenatal range now includes the first IVDR-certified probe kit.

Features of our Prenatal range:

- Larger 30 test and 50 test packs for the most commonly performed investigations
- The option of a 2-hour protocol with *FAST* Prenatal Kits
- First IVDR-certified probe kit

References

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Prenatal FISH Probe Range

Probe Description	Chromosome Region		No. Tests	Cat. No.*
X, Y, 18, 13 and 21	Probe Set 1	X centromere Xp11.1-q11.1 (DXZ1) Green	5, 10, 30 or 50	*FAST* FISH: LPF 001 Standard: LPA 001
		Y centromere Yp11.1-q11.1 (DYZ3) Orange		
		18 centromere 18p11.1-q11.1 (D18Z1) Blue		
	Probe Set 2	13 unique sequence (13q14.2) Green		
		21 unique sequence (21q22.1) Orange		
X, Y and 18	X centromere Xp11.1-q11.1 (DXZ1) Green		5 or 10	*FAST* FISH: LPF 002 Standard: LPA 002
	Y centromere Yp11.1-q11.1 (DYZ3) Orange			
	18 centromere 18p11.1-q11.1 (D18Z1) Blue			
13 and 21	13 unique sequence (13q14.2) Green		5 or 10	*FAST* FISH: LPF 003
	21 unique sequence (21q22.1) Orange			
IVDR 13 and 21	13 unique sequence (13q14.2) Green		5 or 10	Standard: CE-LPA 003
	21 unique sequence (21q22.1) Orange			
13, 18 and 21	13 unique sequence (13q14.2) Green		5 or 10	LPA 005
	18 centromere 18p11.1-q11.1 (D18Z1) Blue			
	21 unique sequence (21q22.1) Orange			
18 Centromere	18 centromere 18p11.1-q11.1 (D18Z1) Blue		5 or 10	LPA 004

*For 5, 30 or 50 test kit, add -X to the catalogue number e.g LPF ###-S, LPF ###-30, LPF ###-50.

CytoCell

Microdeletion and Prenatal FISH Probes

Ordering information

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Microdeletion Probe Range

Probe Name	Chromosome Region	No. Tests	Cat. No.[†]
Angelman (UBE3A/D15S10)	15q11.2-q12	5 or 10	LPU 006
Cri-du-chat and SOTOS Probe Combination	5p15.3/5p15.2/5q35.2	5 or 10	LPU 013
DiGeorge II (10p14)	10p14	5 or 10	LPU 015
DiGeorge/VCFS N25 & 22q13.3 Deletion Probe Combination	22q11.2/22q13.3	5 or 10	LPU 010
DiGeorge/VCFS TUPLE1 & 22q13.3 Deletion Probe Combination	22q11.2/22q13.3	5 or 10	LPU 004
DiGeorge/TBX1 & 22q13.3 Deletion Probe Combination	22q11.2/22q13.3	5 or 10	LPU 014
Kallmann (KAL1)/STS Probe Combination	Xp22.31	5 or 10	LPU 016
Prader-Willi/Angelman (SNRPN)	15q11.2	5 or 10	LPU 005
Saethre-Chotzen/Williams-Beuren Probe Combination	7p21/7q11.23	5 or 10	LPU 024
SHOX Probe	Xp22.33/Yp11.32	5 or 10	LPU 025
Smith-Magenis (RAI1)/Miller-Dieker Probe Combination	17p13/17p11.2	5 or 10	LPU 019
SRY Probe	Yp11.31/ Yq12	5 or 10	LPU 026
Williams-Beuren Probe	7q11.23	5 or 10	LPU 011
Wolf-Hirschhorn (WHSCR) Probe	4p16.3	5 or 10	LPU 009

[†]For 5 test kit add -S to catalogue number, e.g: LPU ###-S.

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What binds us, makes us.

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