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Summary of Safety & Effectiveness
Cholesterol 1,2,3™

K014018

1.0 Submitted By:
Thomas M. Tsakeris
Devices & Diagnostics Consulting Group, Inc.
16809 Briardale Road
Rockville, MD 20855
Phone: 301-330-2076
Fax: 301-330-2568
E-mail: ttsak@erols.com

2.0 Date Submitted:
May 30, 2002

3.0 Device Name:
Cholesterol 1,2,3™

4.0 Predicate Devices:

Predicate	Manufacturer	Docket Number
Synchron CX® Systems HDL Cholesterol Reagent	Beckman Instruments, Inc.	K895851
HDL Cholesterol Plus	Roche Diagnostics Corporation	K000568

5.0 Description:
The Cholesterol 1,2,3™ spectrophotometer in conjunction with the Cholesterol 1,2,3™ reagents are intended for use in the quantitative determination of cholesterol in the epidermal layer of the skin.

6.0 Intended Use and Indications for Use:
6.1 Intended Use:
Cholesterol 1,2,3™ is an *in vitro* diagnostic test for the quantification of skin cholesterol. Cholesterol 1,2,3™ uses a detector reagent that reacts with skin cholesterol in proportion to the amount of cholesterol on the surface of the epidermis. An indicator reagent (horseradish peroxidase substrate) is added and color allowed to develop. Color intensity is proportional to the amount of bound skin cholesterol in the palmar surface of the skin. The color intensity (hue) can be measured objectively by use of a handheld reflectance spectrophotometer.

6.2 Indications for Use:
Skin cholesterol as measured by Cholesterol 1,2,3™ can be used as part of risk assessment for coronary heart disease in persons with a history of myocardial infarction and/or in persons suspected of having significant multi-vessel coronary artery disease (>50% stenosis in >1 vessel as diagnosed by coronary angiography) where further diagnostic evaluation is being considered. Test results, when considered in conjunction with clinical evaluation, blood cholesterol tests and other risk factors identified for coronary artery disease, will aid the physician in focusing diagnostic and patient management options.

7.0 Summary of Performance Data

Skin cholesterol levels were measured in 750 individuals (649 patients scheduled for coronary angiography and 101 age and gender matched controls). The patients were mostly Caucasian. For the 649 case patients who underwent coronary angiography, three coronary arteries (LAD, LCX and RCA) were scored as having no stenosis, up to 50% stenosis and greater than 50% stenosis.

As shown in Figure 1 and Table 1, the risk of significant multi-vessel coronary artery disease (>50% stenosis in >1 vessel) increased as skin cholesterol levels increased in subjects with HDL levels less than 41 mg/dL. In subjects with HDL levels greater than 41 mg/dL the risk of multi-vessel disease was highest in the middle skin cholesterol tertile. The prevalence of significant multi-vessel coronary artery disease for angiography patients in this study was 36.5% (237/649).

Figure 1. Relative Risks of Significant Multi-Vessel Coronary Artery Disease (>50% stenosis in >1 vessel) According to Skin Cholesterol Tertile and HDL Range (the risk of significant multi-vessel coronary artery disease for subjects with HDL<41 is considered as one). Units of measure for skin cholesterol and HDL are hue angle (h^0) and mg/dL respectively.

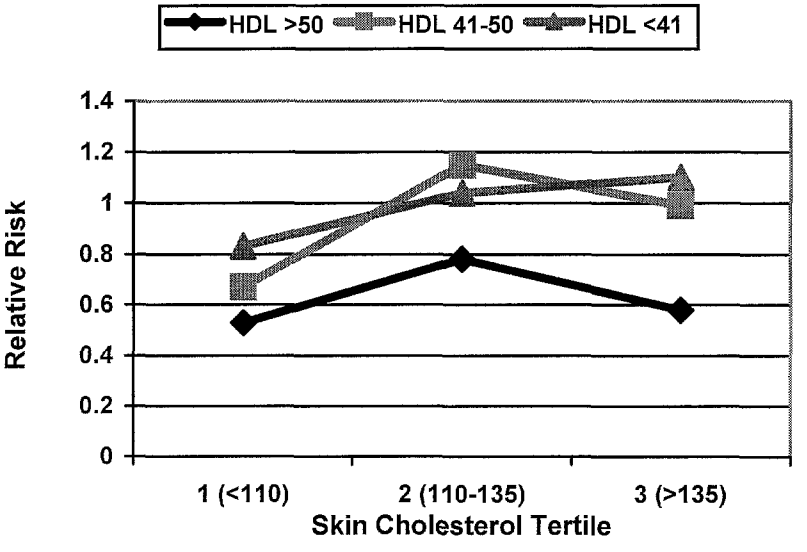


Table 1. Data presented in Figure 1 are shown in this table. Data are presented as average relative risks of significant multi-vessel disease with 95% confidence intervals and ratios of number of patients with significant multi-vessel disease to total number (the risk of significant multi-vessel coronary artery disease for subjects with HDL<41 is considered as one).

	Skin Cholesterol (SC) Level (hue angle)			
HDL Level (mg/dL)	**<110**	**110-135**	**>135**	**Average Relative Risk for HDL Group**
>50	**0.53** (0.29; 0.85) (12/56)	**0.78** (0.48; 1.12) (17/54)	**0.58** (0.27; 1.01) (8/34)	**0.63** (0.47; 0.83) (37/144)
41-50	**0.67** (0.40; 1.01) (15/55)	**1.15** (0.78; 1.53) (21/45)	**0.99** (0.67; 1.33) (22/55)	**0.92** (0.74; 1.12) (58/155)
<41	**0.83** (0.62; 1.07) (37/109)	**1.04** (0.82; 1.28) (50/118)	**1.10** (0.88; 1.33) (55/123)	**1** (142/350)
Average Relative Risk for SC Group	**0.72** (0.57; 0.88) (64/220)	**1.00** (0.84; 1.17) (88/217)	**0.99** (0.83; 1.16) (85/212)	

The logistic regression analysis of skin cholesterol and HDL levels as risks factors for significant multi-vessel coronary artery disease showed that the skin cholesterol had statistically significant contribution (p=0.01) to the risk of significant multi-vessel disease even after adjusting for HDL cholesterol. The area under receiver operating characteristics curve for the skin cholesterol was 0.56 with 95% confidence interval of 0.52-0.61.

Figure 2 and Table 2 show that the probability to have prior myocardial infarction (MI) increased as skin cholesterol increased in individuals with low HDL levels. In subjects with HDL levels >41 mg/dL, history of MI was lowest in the first skin cholesterol tertile and highest in second tertile. The prevalence of history of MI for angiography patients in this study was 34.7% (225/649).

Figure 2. Relative Risks of Prior Myocardial Infarction (MI) According to Skin Cholesterol tertile and HDL range (the risk of prior MI for subjects with HDL<41 is considered as one). Units of measure for skin cholesterol and HDL are hue angle (h^0) and mg/dL respectively.

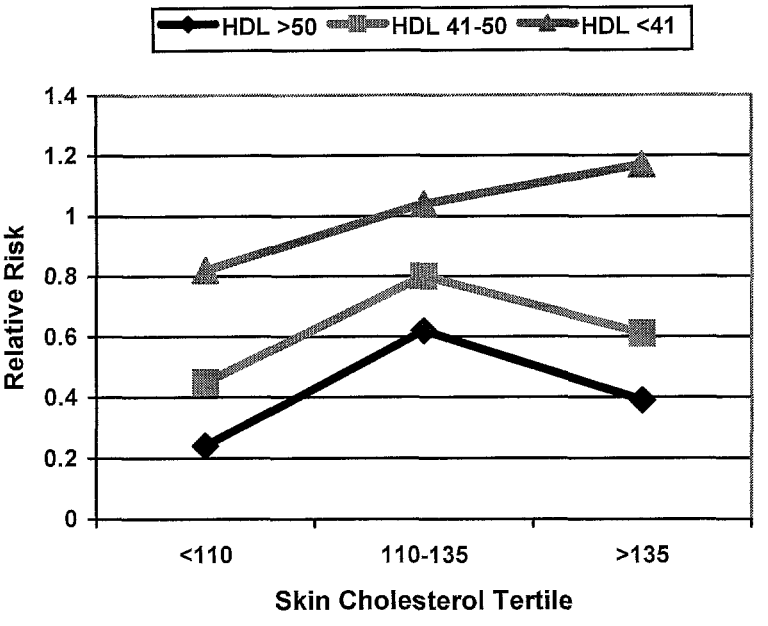


Table 2. Data presented in Figure 2 are shown in this table. Data are presented as average relative risks of prior MI with 95% confidence intervals and ratios of number of patients with prior MI to total number (the risk of prior MI for subjects with HDL < 41 is considered as one).

	Skin Cholesterol (SC) Level (hue angle)			
HDL Level (mg/dL)	**<110**	**110-135**	**>135**	**Average Risk for HDL Group**
>50	**0.24** (0.09; 0.49) (6/56)	**0.62** (0.37; 0.93) (15/54)	**0.39** (0.15; 0.78) (6/34)	**0.42** (0.28; 0.59) (27/144)
41-50	**0.45** (0.23; 0.74) (11/55)	**0.80** (0.49; 1.15) (16/45)	**0.61** (0.36; 0.92) (15/55)	**0.61** (0.46; 0.78) (42/155)
<41	**0.82** (0.62; 1.07) (40/109)	**1.04** (0.78; 1.20) (52/118)	**1.17** (0.96; 1.37) (64/123)	**1** (156/350)
Average Risk for SC Group	**0.58** (0.46; 0.72) (57/220)	**0.91** (0.71; 1.01) (83/217)	**0.90** (0.75; 1.05) (85/212)	

Figure 3 and Table 3 show that the angiography patients with low skin cholesterol (<110) and high HDL (>50 mg/dL) had the highest probability of being without disease (no stenosis at any three arteries). Conversely, the patients with high skin cholesterol (>135) and low HDL (<41 mg/dL) had the lowest probability of being without disease. However, skin cholesterol level cannot be used to rule out coronary artery disease as even in the lowest skin cholesterol tertile significant percentages of subjects had coronary artery disease (only 26.9% of angiography subjects with skin cholesterol (<110) were without stenosis at three arteries). The skin cholesterol test cannot be used to screen the general population for no CAD. The

prior probability (prevalence) of no disease for angiography patients in this study was 23.6% (153/649).

Figure 3. Probability of No Coronary Artery Disease According to Skin Cholesterol Tertile and HDL Range. Units of measure for skin cholesterol and HDL are hue angle (h^0) and mg/dL respectively.

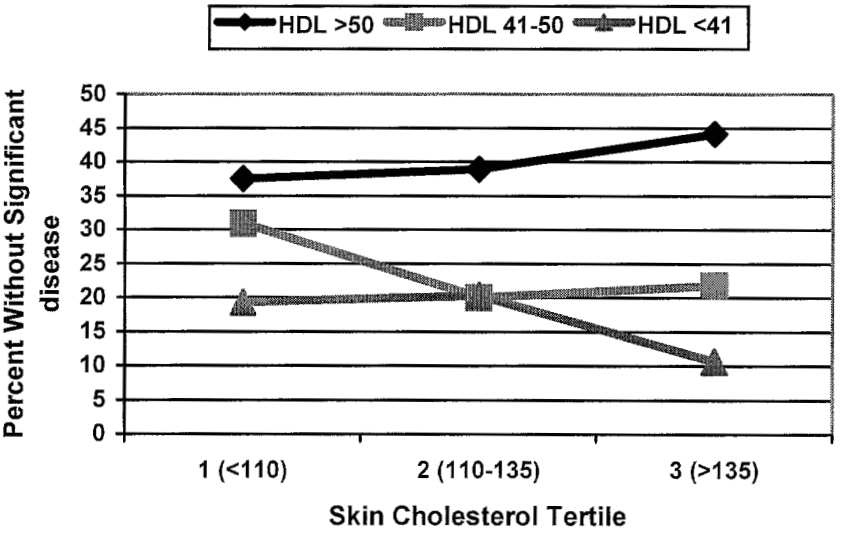


Table 3. Data presented in Figure 3 are shown in this table. Data are presented as average percent without coronary artery disease (no stenosis at any three arteries) with 95% confidence intervals.

	Skin Cholesterol (SC) Level (hue angle)			
HDL Level (mg/dL)	**<110**	**110-135**	**>135**	**Average Risk for HDL Group**
>50	**37.5%** (21/56) (24.9%; 51.5%)	**38.9%** (21/54) (25.9%; 53.1%)	**44.1%** (15/34) (27.2%; 62.1%)	**39.6%** (57/144) (31.5%; 48.1%)
41-50	**30.9%** (17/55) (19.1%; 44.8%)	**20.0%** (9/45) (9.6%; 34.6%)	**21.8%** (12/55) (11.8%; 35.0%)	**24.5%** (38/155) (18.0%; 32.1%)
<41	**19.3%** (21/109) (12.3%; 27.9%)	**20.3%** (24/118) (13.5%; 28.7%)	**10.6%** (13/123) (5.8%; 17.4%)	**16.6%** (58/350) (12.8%; 20.9%)
Average Risk for SC Group	**26.9%** (59/220) (21.1%; 33.2%)	**24.9%** (54/217) (19.3%; 31.2%)	**18.9%** (40/212) (13.8%; 24.8%)	

As shown in table 4, data of this study demonstrated that there is no correlation of skin cholesterol with HDL (coefficient of correlation = - 0.06 with 95% confidence interval (-0.15; 0.02)).

Table 4. Distribution of Skin Cholesterol Levels and HDL Concentration.

	Skin Cholesterol (SC) Level (hue angle)			
HDL Level (mg/dL)	**<110**	**110-135**	**>135**	
>50	8.6% 56	8.3% 54	5.2% 34	22.2% 144
41-50	8.5% 55	6.9% 45	8.5% 55	23.9% 155
<41	16.8% 109	18.2% 118	19.0% 123	53.9% 350
	33.9% 220	33.4% 217	32.7% 212	100% 649

8.0 Specific Performance Characteristics

8.1 Precision

Table 1 shows the reproducibility of Cholesterol 1,2,3™ within-day, between days, and from batch to batch.

Table 1. Reproducibility of Cholesterol 1,2,3™: Mean CV (range)

	Within-Day	Day-to-Day	Batch-to-Batch[a]
Low skin cholesterol	11% (5-19%)	8% (4-17%)	10% (1-17%)
High skin cholesterol	7% (2-13%)	3% (1-5%)	

[a] *3 lots of Cholesterol 1,2,3™ were compared*

For within day variability, three replicate Cholesterol 1,2,3™ tests were carried out on the palmar surface of each hand on twenty candidates (10 individuals in each of the low and high skin cholesterol ranges) with a single lot of Cholesterol 1,2,3™. Three different areas of the palm were used. For day-to-day variability, a single Cholesterol 1,2,3™ test was carried out on twenty candidates (10 individuals in each of the low and high skin cholesterol ranges) for 5 consecutive days. A single lot of Cholesterol 1,2,3™ was used. For between lot variability, ten candidates were tested with three different Cholesterol 1,2,3™ kit lots. All three tests for each individual were performed on the same day on three different areas of the palm.

8.2 Skin Cholesterol Values in Healthy Subjects

Table 6 shows the levels of skin cholesterol in the control Caucasian and African-American populations. The mean skin cholesterol values for these healthy subjects are within the lowest tertile of the angiographic subjects (<110).

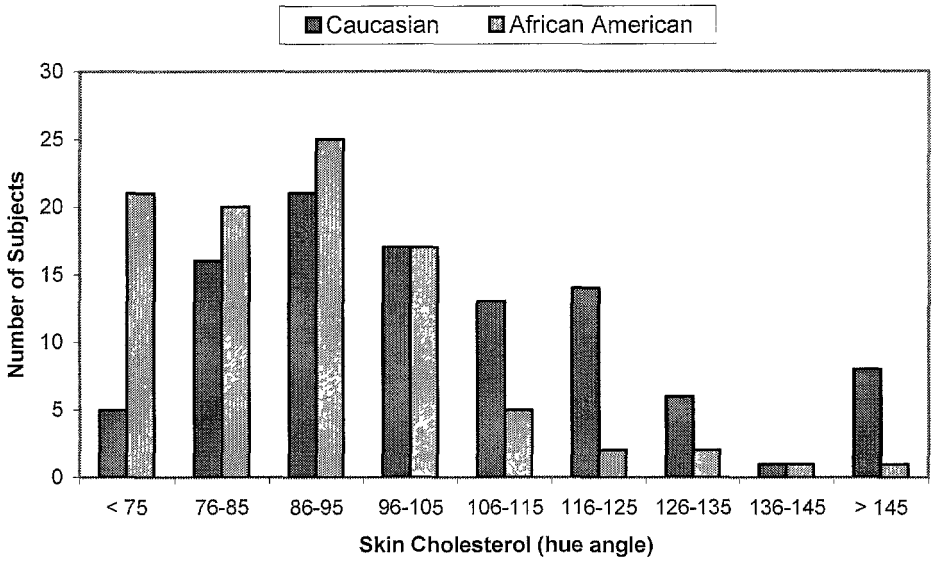
Table 6. Expected Skin Cholesterol Values in Control Subjects

	Caucasians*	African Americans**
N	101	94
Mean	105.0	88.7
2.5 percentile	66	62
97.5 percentile	169	131

* mean age: 61 (40-82), 41% female
** mean age 42 (19-70), 79% female

Figure 4 shows the distribution of skin cholesterol for the control population by race.

Figure 4. Distribution of Skin Cholesterol by Race



This summary of safety and effectiveness is being submitted in accordance with the requirements of the Safe Medical Device Act of 1990 and the implementing regulation 21 CFR 807.92.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 2 4 2002

International Medical Innovation, Inc.
c/o Thomas M. Tsakeris
President Devices & Diagnostics Consulting Group, Inc.
16809 Briardale Road
Rockville, MD 20855

Re: k014018
Trade/Device Name: Cholesterol 1,2,3™
Regulation Number: 21 CFR 862.1475
Regulation Name: Lipoprotein test system
Regulatory Class: I, reserved
Product Code: LBS
Dated: May 31, 2002
Received: May 31, 2002

Dear Mr. Tsakeris:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act and the limitations described below. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

The Office of Device Evaluation has determined that there is a reasonable likelihood that this device will be used for an intended use not identified in the proposed labeling and that such use could cause harm. Therefore, in accordance with Section 513(i)(1)(E) of the Act, the following limitation must appear in the Warnings section of the device's labeling:

> The safety and effectiveness of this device for use in screening the general population for coronary artery disease or for use as a substitute for blood cholesterol tests or a substitute for other risk factors identified for coronary artery disease have not been established.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and permits your device to proceed to the market. This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification if the limitation statement above is added to your labeling, as described.

Please note that the above labeling limitations are required by Section 513(i)(1)(E) of the Act. Therefore, a new 510(k) is required before these limitations are modified in any way or removed from the device's labeling.

If you desire specific information about the application of other labeling requirements to your device (21 CFR Part 801 and additionally Part 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4616. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification"(21 CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Bernard E. Statland, M.D., Ph.D.
Director
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K014018

Device Name: Cholesterol 1,2,3™

Intended Use Statement
Cholesterol 1,2,3™ is an *in vitro* diagnostic test for the quantification of skin cholesterol. Cholesterol 1,2,3™ uses a detector reagent that reacts with skin cholesterol in proportion to the amount of cholesterol on the surface of the epidermis. An indicator reagent (horseradish peroxidase substrate) is added and color allowed to develop. Color intensity is proportional to the amount of bound skin cholesterol in the palmar surface of the skin. The color intensity (hue) can be measured objectively by use of a handheld reflectance spectrophotometer.

Indications For Use Statement
Skin cholesterol as measured by Cholesterol 1,2,3™ can be used as part of risk assessment for coronary heart disease in persons with a history of myocardial infarction and/or in persons suspected of having significant multi-vessel coronary artery disease (>50% stenosis in >1 vessel as diagnosed by coronary angiography) where further diagnostic evaluation is being considered. Test results, when considered in conjunction with clinical evaluation, blood cholesterol tests and other risk factors identified for coronary artery disease, will aid the physician in focusing diagnostic and patient management options.

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number: K014018

For Prescription Use √ OR Over-The-Counter Use __
(Per 21 CFR 801.109)

(Optional Format 1-2-96)

A Butnar 6/24/02
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K [redacted] 014018