Recommendations for the testing and reporting of lipids in clinical diagnostic laboratories within the Republic of Ireland. Version 7.0

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Background

The testing and reporting of lipids play an important part in cardiovascular disease (CVD) risk assessment. Chemical Pathologists are uniquely trained in both the laboratory and clinical aspects of lipidology. Accordingly, the Chemical Pathology subgroup of the Faculty of Pathology RCPI has produced the first Irish guidelines for lipid testing and reporting.

Scope

The aim is to provide guidelines for lipid testing and reporting for use by clinicians and clinical laboratories. It follows the laboratory pathway that a sample takes: pre-analytical, analytical and post-analytical and makes recommendations relating to each of these phases.

Abbreviations

HDL-C	HDL cholesterol
LDL-C	LDL cholesterol
TG	Triglycerides

Key recommendations

1. The standard lipid profile should contain serum/plasma total cholesterol, HDL cholesterol (HDL-C), non HDL cholesterol (non HDL-C), triglycerides, and LDL cholesterol (LDL-C).
2. LDL-C can be reported as either a "calculated LDL cholesterol" using the Friedewald equation or analysed by a "direct LDL cholesterol" assay.
3. Each laboratory should state clearly which method of LDL-C is being reported.
4. This standard profile should be provided whenever the following tests are requested to ensure a standard approach for patients: "cholesterol", "fats", "lipids", "lipid profile", "cholesterol profile", and so forth.
5. Fasting is not required for the analysis of the standard lipid profile.

6. Serum and plasma separated within 12 hours are the usual specimen types. Analysis of separated specimens can occur within 7 days if stored at 4-8^{0}C until analysis.
7. The measurement of triglycerides should be considered on the first lipaemic sample in a healthcare episode to help determine the degree of the dyslipidaemia.
8. The acute phase response is known to affect lipid and lipoprotein concentrations and thus lipids and lipoproteins should ideally be requested when a person is well. In general, lipids and lipoproteins should not be measured during a fever or major infection or after major surgery. Ideally, lipids and lipoproteins should be requested as soon as possible within the first 24 hours post an acute coronary syndrome or a stroke. They should ideally not be measured for at least 6 weeks following such clinical events.
9. In general, it is not recommended that lipids or lipoproteins are routinely measured in pregnancy, in the first 6 weeks after pregnancy or immediately after excessive alcohol intake unless pancreatitis is suspected.
10. It is recommended that there should be at least one public hospital laboratory able to analyse the following specialist lipid assays for specialist lipid management:
    a. Familial Hypercholesterolaemia (FH) mutation detection
    b. Serum/Plasma Lipoprotein (a)
    c. Serum/Plasma Apolipoprotein B
    d. Serum/Plasma Apolipoprotein AI
    e. Apolipoprotein E genotyping
    f. Lipoprotein electrophoresis
    g. Beta quantification/ultracentrifugation

Epidemiology

Raised total cholesterol (≥5.0 mmol/L) is a major cause of vascular disease burden in Ireland. With the prevalence of raised total cholesterol in adults of both genders being ≥60%, Ireland is amongst the countries with the greatest hypercholesterolaemia burden in the world (the global prevalence of raised total cholesterol among adults was 37% for males and 40% for females and the European prevalence was 54% for both genders). In Ireland, a 30% reduction in the heart disease death rate has been attributed to a 4.6% reduction of the population mean for total cholesterol. Average total cholesterol worldwide has decreased by less than 0.1 mmol/L between 1980 and 2008 per decade in men and women.

Testing

Pre-analytical phase

The pre-analytical stage is about doing the right test on the right patient at the right time and is where most errors occur. This is especially the case with lipids in view of the use of calculated values. It also has the potential to be rate limiting especially in primary care if the fasting state is only employed.

1. The recommended standard serum/plasma lipid profile provided by laboratories should contain total cholesterol, HDL cholesterol, non-HDL cholesterol (1, 2), triglycerides and LDL cholesterol. It is important to note that LDL cholesterol can be reported as either a “calculated LDL Cholesterol” using the Friedewald equation (see point 17 for equation) or analysed by a “direct LDL Cholesterol” assay, and therefore each laboratory should state clearly which method of LDL-C is being reported. Furthermore, it is recommended that this profile is provided whenever the following tests are requested by laboratory service

users to ensure a standard approach for patients: “cholesterol”, “fats”, “lipids”, “lipid profile”, “cholesterol profile”, and so forth.

2. Fasting is not required for the analysis of the standard lipid profile and is fully acceptable for CVD risk estimation (3, 4, 5, 17).
    a. The maximal mean changes between fasting and non-fasting states is not clinically significant at +0.3 mmol/L for triglycerides, -0.2 mmol/L for cholesterol, and there is no change in HDL-C (21).
    b. Fasting is beneficial where there is a known elevated triglyceride (e.g. > 4.5 mmol/L, which will also affect the LDL-C calculation) and where another fasting blood test is required such as a fasting glucose.
    c. Non HDL cholesterol is a strong CVD risk indicator and can be calculated in a non-fasting specimen (by subtracting HDL cholesterol from the total cholesterol) and thus can be reported even when triglycerides are high and calculated LDL cholesterol not possible.
3. Serum and plasma separated within 12 hours are the usual specimen types. These specimen types are assumed unless otherwise stated. Analysis of separated specimens can occur within 7 days if stored at 4-8^{0}C until analysis (6).
4. The measurement of triglycerides should be considered on the first lipaemic sample in a healthcare episode to help determine the degree of the dyslipidaemia. This may be by means of an automated process based on the lipaemic index or other procedure (7).
5. The acute phase response is known to affect lipid and lipoprotein concentrations and thus lipids and lipoproteins should ideally be requested when a person is well. In general, lipids and lipoproteins should not be measured during a fever or major infection or after major surgery. Ideally, lipids and lipoproteins should be requested as soon as possible within the first 24 hours post an acute coronary syndrome (8) or a stroke. They should not be measured for at least 6 weeks following such clinical events (8).
6. In general, it is not recommended that lipids or lipoproteins are routinely measured in pregnancy, in the first 6 weeks after pregnancy or right after excessive alcohol intake unless pancreatitis is suspected (9).

Who to Test

7. As ≥60% of the Irish population has hypercholesterolaemia, lipids should be requested during opportunistic and planned cardiovascular disease (CVD) risk assessment. Patients presenting with new onset CVD should be checked upon admission.

Who to Re-Test and Re-Testing Intervals

8. As ≥60% of the Irish population has hypercholesterolaemia, lipids should be requested during opportunistic and planned cardiovascular disease (CVD) risk assessment. Patients presenting with new onset CVD should be checked upon admission.
9. The dose of LDL cholesterol lowering medications should be individualised according to baseline LDL-C levels, the goal of therapy, and patient response. Accordingly, patients on LDL cholesterol lowering medications will require lipid testing based on their individual clinical scenario.

10. Re-testing intervals must not only reflect the analyte being requested, but also how it is being used - thus they must also reflect local protocols. Clearly, clinicians can decide otherwise if they feel that it is clinically appropriate to request a test more or less frequently based on the clinical scenario in question. This is especially the case in CVD risk prevention due to the large biological variability of lipids (18). Testing also encourages patient awareness and participation in the management of their CVD risk. The availability of all previously reported laboratory results at or before the time of requesting a new test should greatly assist the clinician in deciding whether a test was appropriate.

Who Not to Test

11. In general, it is not recommended that lipids or lipoproteins are routinely measured in pregnancy, in the first 6 weeks after pregnancy or immediately after excessive alcohol intake unless pancreatitis is suspected.
12. It should be noted that the maximum therapeutic response for HMGCoA reductase inhibitors (statins) is usually achieved within 4 weeks. Similarly, the adjustment of statin dose should be made at intervals of 4 weeks or more. Accordingly, there is little benefit in rechecking within 4 weeks.

How to Test

Analytical phase

This phase is about getting the right result. More has been written about the analytical phase than both other phases combined. Not surprisingly, this is the most regulated phase of all the three phases of laboratory operations. It is also the phase with the greatest evidence base.

13. All labs analysing lipids, lipoproteins and a lipaemic index should perform Internal Quality Control using third party materials (10).
14. Laboratories should participate in an EQA programme for lipids and lipoproteins that is designed and overseen by appropriately competent professionals including clinical oversight. The distribution frequency should be at least monthly with commutable specimens that cover the whole clinical range and especially any clinical cut-offs for the assay employed. Each distribution cycle should include sufficient samples to provide evidence of reproducibility; selected distributions should include ‘challenging’ samples; and educational input. EQA samples should be ‘blinded’ to participants in relation to expected results with the samples treated as much as possible as if they were patient samples. Ideally, the EQA programme should be an accredited programme and should participate in post marketing vigilance with the appropriate national competent authority for in vitro diagnostics (11).
15. Triglyceride assays that measure triglyceride associated glycerol and not total glycerol are ideally recommended (12) to avoid pseudo-hypertriglyceridaemia (13).
16. Each laboratory should check its HDL-C assay ‘Instructions For Use’ for the potential effect of raised triglycerides, typically >11.3 mmol/L, on the quality of the results produced and take this into account (14).

17. For laboratories providing direct LDL-C assays, they should check the 'Instructions For Use' for the potential effect of raised triglycerides on the quality of the results produced and take this into account.
18. For calculated LDL-C, the recommended Friedewald equation calculation that should be employed is the original equation:

    Calculated LDL-C = total cholesterol – HDL cholesterol – triglycerides / 2.2 (15)

19. The maximum recommended triglyceride concentration above which the calculated LDL-C should not be provided is 4.5 mmol/L (15)
20. The use of calibrators that have assigned values that are traceable to the United States Centres for Disease Control (US CDC) reference methods are recommended.
21. SI units are recommended for reporting of results, that is, mmol/L.
22. Total cholesterol, HDL-C, triglycerides and LDL-C should be reported to a single decimal place (4).
23. It is recommended that there should be at least one public hospital laboratory able to analyse the following specialist lipid assays for specialist lipid management:
    a. Familial Hypercholesterolaemia (FH) mutation detection
    b. Serum/Plasma Lipoprotein (a)
    c. Serum/Plasma Apolipoprotein B
    d. Serum/Plasma Apolipoprotein AI
    e. Apolipoprotein E genotyping
    f. Lipoprotein electrophoresis
    g. Beta quantification/ultracentrifugation

    Hospitals that provide such tests include:

Test	**Laboratory**
FH mutation detection	Biochemistry Department, St James Hospital
Apolipoprotein E genotyping	Biochemistry Department, St. James's Hospital
Lp(a)	Tallaght, SVUH from 2017
Apo B	Tallaght, SVUH from 2017
Apo AI	Tallaght, SVUH from 2017
Lipoprotein electrophoresis	Tallaght (Quantimetrix system) City Hospital Nottingham NG5 1PB, or St Thomas' Hospital, London SE1 7EH
Beta quantification / ultracentrifugation	Glasgow Royal Infirmary, Glasgow G4 0SF St Thomas' Hospital, London SE1 7EH

24. A completed standard laboratory test request form must be sent with all samples.

Information required on the referral form

25. The request form must include detailed patient and clinical information including:

    - **Patient demographics**
      - Patient's Name

- Patient's Date of Birth
- Medical Record Number
- Name of Referring Clinician
- Name of Referring Hospital
- Order number / external laboratory number (if applicable to external agencies only).

- **Request details**
  - Example - Clinical indication for testing (see list above)
  - Example - Details of any medications

Requests received with no clinical details or with inadequate patient demographics will not be analysed

26. Full clinical information should accompany all requests. In the event a request is received which does not have the required data (above) or does not have adequate clinical details the laboratory could:
27. Issue a report to the requesting doctor, requesting additional clinical details and/or advise that the case is discussed with the local Laboratory Medicine Consultant, and advising that the sample will be discarded after 7 days if there is no reply
28. Store the sample for up to 7 days awaiting further communication from the referring clinician
29. Samples can be discarded after 7 days if the referring clinician has not provided the required details or if it is determined that testing is not indicated.

Interpretation of tests
Post-analytical phase

This phase is about facilitating the correct interpretation and ensuring effective clinical action. Laboratories should ideally be a source of knowledge to underpin, assist and support the appropriate interpretation of lipid results. This is aided by laboratories providing clinical interpretative reports.

30. When a triglyceride concentration is ≥4.5 mmol/L, it is recommended that a comment is appended to the report advising the requester to consider a repeat fasting profile if the initial request related to a non-fasting sample.
31. When a triglyceride concentration is >10 mmol/L, it is recommended than consideration is given to notifying the requester of the possible risk of acute pancreatitis associated with severe hypertriglyceridaemia (17), e.g. *"High Triglycerides > 10 mmol/L – risk of pancreatitis"*

32. It is recommended that patients at high risk of CVD, including those at high risk of Familial Hypercholesterolaemia due to their LDL-Cholesterol concentration being ≥5.0 mmol/L, are highlighted to laboratory service users by means of an automated laboratory comment appended to the report or by another process. An example of such a comment is *"Significantly elevated LDL-cholesterol – patient at high risk of CVD. If there is a personal or family history of premature vascular disease then this patient may have Familial Hypercholesterolaemia".*

33. The following ESC/EAS clinical action points are recommended (17):
    a. For patients with very high CVD risk, the treatment target for LDL-C is <1.8 mmol/L (non HDL-C <2.6 mmol/L) or a reduction of at least 50% if the baseline LDL-C is between 1.8 and 3.5 mmol/L is recommended;
    b. For patients with a high CVD risk, an LDL-C level of <2.6 mmol/L (non HDL-C <3.4 mmol/L) or a reduction of at least 50% if the baseline LDL-C is between 2.6 and 5.2 mmol/L is recommended;
    c. For patients at moderate CVD risk, an LDL-C target of <3.0 mmol/L (non HDL-C <3.8 mmol/L) should be considered.

34. Non-HDL-cholesterol cut-offs are generally 0.8 mmol/L higher than the respective LDL-cholesterol cut-offs.
35. Appropriate age-related acceptable limits for children with calculated LDL-Cholesterol using the Friedewald equation are provided by the NHLBI Guidelines (20)
36. It is good practice to do an annual audit of the performance of laboratory calculations to verify that the equations remain valid. This also applies to calculated LDL-C, non HDL-C and similarly derived indices.
37. Recommended cut-points for reporting of lipid results are shown in the following table (21), along with CVS guidelines cut-points, and “extremely abnormal “ cutpoints for flagging and commenting (basis of a quick reference card):

Recommended cut-points for flagging lipid results

Standard Lipid Profile Result	Non-Fasting	Fasting	Very abnormal concentrations requiring specific commenting (regardless of whether fasting or non-fasting) and discussion with a lipidologist
Triglycerides	≤ 2.0 mmol/L	≤ 1.7 mmol/L	≥10 mmol/L (risk of pancreatitis)
Total cholesterol	≤ 5.0 mmol/L	≤ 5.0 mmol/L	≥ 7.5 mmol/L especially if family history, - risk of FH (22)
HDL cholesterol (gender-specific cutpoints are also available)	≤ 1.0 mmol/L	≤ 1.0 mmol/L	≤ 0.3 mmol/L (possibility of genetic causes)
LDL cholesterol	≤ 3.0 mmol/L	≤ 3.0 mmol/L	≥5 mmol/L (may indicate heterozygous FH with increase CVD risk) ≤ 0.3 mmol/L (possibility of genetic causes)
Non HDL cholesterol	≤ 3.8 mmol/L	≤ 3.8 mmol/L	

Cardiovascular Disease Risk Assessment Tools

There are a number of well validated cardiovascular disease risk assessment systems available that are recommended as part of different guidelines. The 2016 European Guidelines on cardiovascular disease prevention in clinical practice (19) provide a list of commonly used tools and the authorities recommending them. While we do not have a consensus recommendation on which of these systems should be used, it is agreed that these tools can enhance clinical decision making in the primary prevention of cardiovascular disease.

Implications for ICT Systems

IT considerations may limit the implementation of some of these voluntary recommendations in laboratories and hospitals at this point in time. However, with the implementation of the national LIS, a standardised approach will be required for many areas of clinical practice in Ireland. This process will require a standardised name and unit for each laboratory test and possibly standardisation of reference intervals and the number of decimal points to which each test should be reported.

Computer Physician/Provider Order Entry Systems (CPOE) from a number of different suppliers are in use in a number of hospitals nationwide. Few ICT systems are capable of effectively integrating primary/community with secondary care facilities, though there are examples of "bridging" solutions such as Healthlink which is used for laboratory test reporting and other applications (including possibly test ordering). At present in Ireland, there is no national electronic health patient record, and the agreed unique national health identifier will take significant time before it is operational. In order to make progress on appropriate utilisation of laboratory services in the interim, it is necessary to consider the laboratory test ordering modules that are currently available in these different settings.

It is also likely that paper laboratory request forms will continue (e.g. in primary care) until the provision of effective ICT systems improves. Improved forms in some cases may help to encourage better provision of relevant clinical information.

Laboratory Test Requesting Modules in Primary Care

It is recommended that user-friendly GP ordering for lipids is developed and implemented at the point of ordering in GP Information Systems. The information required for requesting lipids is as stated above, and a user-friendly screen should be developed to allow the GP to select one or more of the relevant clinical indications and to indicate relevant drug therapy. This will require discussion with GP system suppliers.

Laboratory Test Requesting Modules in Hospital-based CPOE systems

CPOE systems from a number of different suppliers are available in several hospitals nationwide. The national MedLIS will also provide an order-entry system. It is recommended that user-friendly screens for ordering lipids is developed and implemented at the point of ordering. The information required for requesting lipids is as stated above, and a user-friendly screen should be developed to allow the GP to select one or more of the relevant clinical indications and to indicate relevant drug therapy.

National Laboratory Information System (MedLIS)

The recommendations given for Primary Care and Hospital-based CPOE systems would apply to circumstances where MedLIS will be providing the CPOE functionality (e.g. where its test ordering Module is implemented throughout the hospital)

A pre-laboratory Module in MedLIS should check for (1) absence of any clinical details; (2) repeat testing; (3) correct indication for testing provided, and generate an alert and an appropriate laboratory report as described above.

References

1. Preiss D, Neely D. Biochemistry laboratories should routinely report non-HDL-cholesterol. Ann Clin Biochem 2015**;** 52: 629-631. 10.1177/0004563215594818
2. Twomey P. Significant hypertriglyceridaemia and HDL cholesterol assays. Ann Clin Biochem 2016 Mar 8. Epub 2016 Mar 8.
3. Fasting Time and Lipid Levels in a Community-Based Population. A Cross-sectional Study. Sidhu D and Naugler C. Arch Intern Med. 2012; 172(22):1707-1710. doi:10.1001/archinternmed.2012.3708
4. Fasting for Lipid Testing - Is It Worth the Trouble? Khera AV and Mora S. Arch Intern Med. 2012; (22):1710-1712. doi:10.1001/2013.jamainternmed.263
5. Lipids and cardiovascular disease 3: Triglycerides and cardiovascular disease. *Børge G Nordestgaard, Anette Varbo. Lancet* 2014; 384: 626–635.
6. Heins M, Heil W, Withold W. Storage of serum or whole blood samples? Effects of time and temperature on 22 serum analytes. Eur J Clin Chem Clin Biochem 1995; 33: 231-8.
7. Twomey PJ, Don-Wauchope AC, McCullough D. Unreliability of triglyceride measurement to predict turbidity induced interference. J Clin Pathol 2003; 56: 861-2.
8. The modification of serum lipids after acute coronary syndrome and importance in clinical practice. Balci B. Current Cardiology Reviews 20011, 7: 272-276.
9. Labtests on line http://labtestsonline.org.uk/understanding/analytes/lipid/tab/test (last accessed 25/11/2016)
10. Kinns H, Pitkin S, Housley D, Freedman DB. Internal quality control: best practice. J Clin Pathol. 2013; 66:1027-32.
11. James D, Ames D, Lopez B, Still R, Simpson W, Twomey P. External quality assessment: best practice. J Clin Pathol 2014; 67: 651-5.
12. TG Cole. Glycerol blanking in triglyceride assays. Clin Chem 1990; 36: 1267-1268.
13. Walmsley TA, Potter H, George PM and Florkowski CM. Pseudo-hypertriglyceridaemia: A measurement artefact due to glycerol kinase deficiency. Postgraduate medical journal 2008; 84: 552-4.
14. Twomey PJ, Pledger DR. HDL-cholesterol and triglycerides: an overlooked issue? J Clin Pathol 2007; 60: 1065-6.
15. Friedewald T, Levy RI, Fredrickson DS. Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma, Without Use of the Preparative Ultracentrifuge Clinical Chemistry 1972; 18:499-502.
16. http://www.pathologyharmony.co.uk/Combined%20Harmony%20units%20spreadsheet%20anonomised%20revised%202012%20(2).pdf last accessed 25/11/2016.
17. ESC/EAS Guidelines for the management of dyslipidaemias. European Heart Journal (2016) 37, 2999–3058 DOI: http://dx.doi.org/10.1093/eurheartj/ehw272 http://eurheartj.oxfordjournals.org/content/early/2016/08/26/eurheartj.ehw272 last accessed 25/11/2016.
18. Reynolds TM, Twomey P, Wierzbicki AS. Accuracy of cardiovascular risk estimation for primary prevention in patients without diabetes. J Cardiovasc Risk 2002; 9:183-90.
19. Massimo F. Piepoli, Arno W. Hoes, Stefan Agewall, Christian Albus, Carlos Brotons, Alberico L. Catapano, Marie-Therese Cooney, Ugo Corrà, Bernard Cosyns, Christi Deaton, Ian Graham, Michael Stephen Hall, F. D. Richard Hobbs, Maja-Lisa Løchen, Herbert Löllgen, Pedro Marques-Vidal, Joep Perk, Eva Prescott, Josep Redon, Dimitrios J. Richter, Naveed Sattar, Yvo Smulders, Monica Tiberi, H. Bart van der Worp, Ineke van Dis, W. M. Monique Verschuren. 2016 European Guidelines on cardiovascular disease prevention in clinical practice Eur Heart J (2016) ehw106 DOI: http://dx.doi.org/10.1093/eurheartj/ehw106 last accessed 25/11/2016.
20. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. Pediatrics 2011; 128: S213-S256. https://www.nhlbi.nih.gov/files/docs/peds_guidelines_sum.pdf
21. Børge G. Nordestgaard, Anne Langsted, Samia Mora, Genovefa Kolovou, Hannsjörg Baum, Eric Bruckert, Gerald F. Watts, Grazyna Sypniewska, Olov Wiklund, Jan Borén, M. John Chapman, Christa Cobbaert, Olivier S. Descamps, Arnold von Eckardstein, Pia R. Kamstrup, Kari Pulkki, Florian Kronenberg, Alan T. Remaley, Nader Rifai, Emilio Ros, Michel Langlois. Fasting Is Not Routinely Required for Determination of a Lipid Profile: Clinical and Laboratory Implications Including Flagging at Desirable Concentration Cutpoints—A Joint Consensus Statement from the European Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine. Clin Chem 2016; 62:930-46
22. Cardiovascular disease: risk assessment and reduction, including lipid modification. National Institute for Health and Care Excellence (NICE) 2014, Clinical Guideline 181.

Quick Reference Card for Lipid Testing

Recommended cut-points for flagging lipid results

Standard Lipid Profile Result	Non-Fasting	Fasting	Very abnormal concentrations requiring specific commenting (regardless of whether fasting or non-fasting) and discussion with a lipidologist
Triglycerides	≤ 2.0 mmol/L	≤ 1.7 mmol/L	≥10 mmol/L (risk of pancreatitis)
Total cholesterol	≤ 5.0 mmol/L	≤ 5.0 mmol/L	≥ 7.5 mmol/L especially if family history, - risk of FH (22)
HDL cholesterol *(gender-specific cutpoints are also available)*	≤ 1.0 mmol/L	≤ 1.0 mmol/L	≤ 0.3 mmol/L (possibility of genetic causes)
LDL cholesterol	≤ 3.0 mmol/L	≤ 3.0 mmol/L	≥5 mmol/L (may indicate heterozygous FH with increase CVD risk) ≤ 0.3 mmol/L (possibility of genetic causes)
Non HDL cholesterol	≤ 3.8 mmol/L	≤ 3.8 mmol/L	

Recommended EAS/ESC Clinical Action Points

Patients with very high CVD risk	The treatment target for LDL-C is <1.8 mmol/L (non HDL-C <2.6 mmol/L) or a reduction of at least 50% if the baseline LDL-C is between 1.8 and 3.5 mmol/L is recommended;
Patients with a high CVD risk	An LDL-C level of <2.6 mmol/L (non HDL-C <3.4 mmol/L) or a reduction of at least 50% if the baseline LDL-C is between 2.6 and 5.2 mmol/L is recommended
Patients at moderate CVD risk	An LDL-C target of <3.0 mmol/L (non HDL-C <3.8 mmol/L) should be considered.